UNIVERSITY OF TORONTO
MEDICAL JOURNAL

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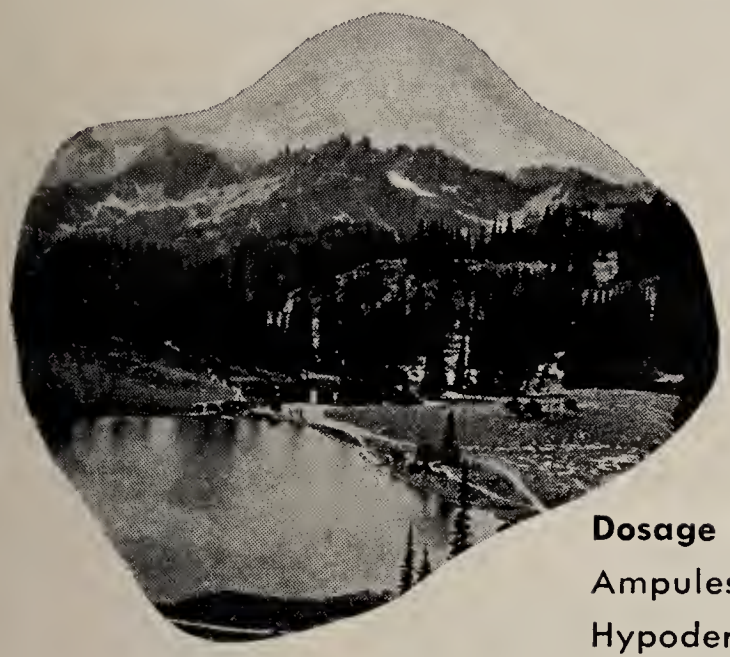

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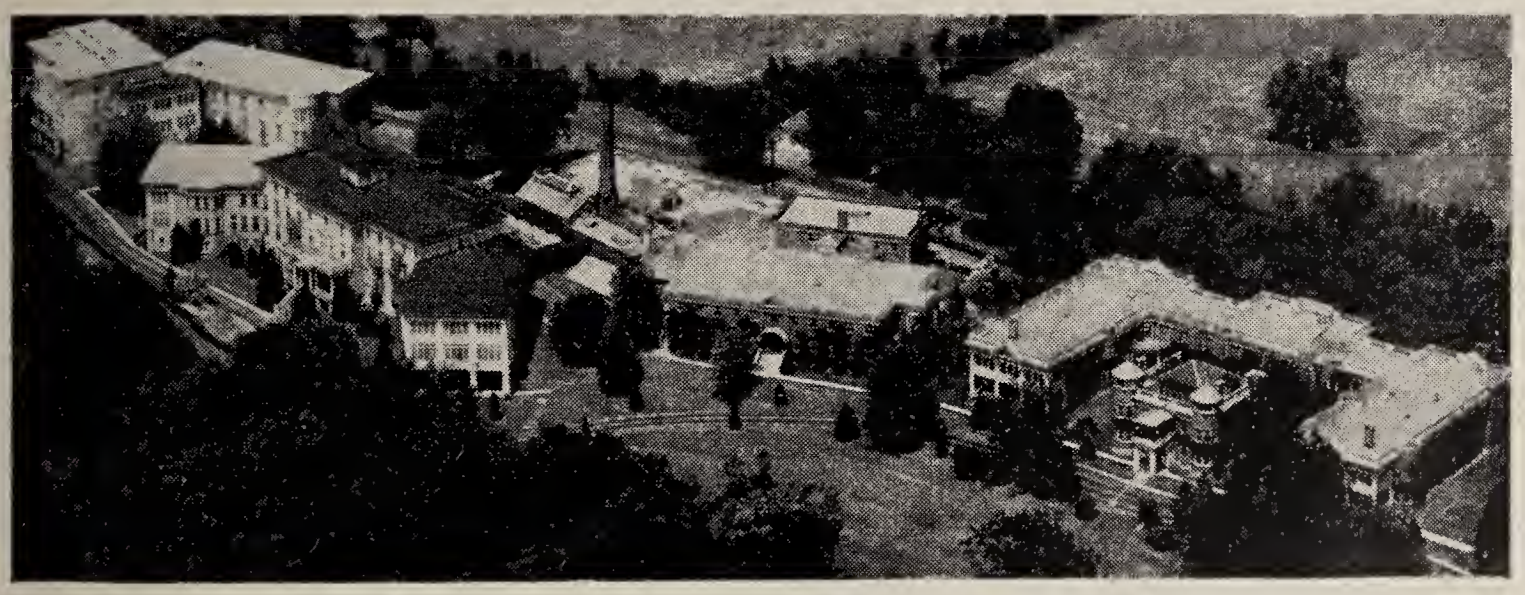

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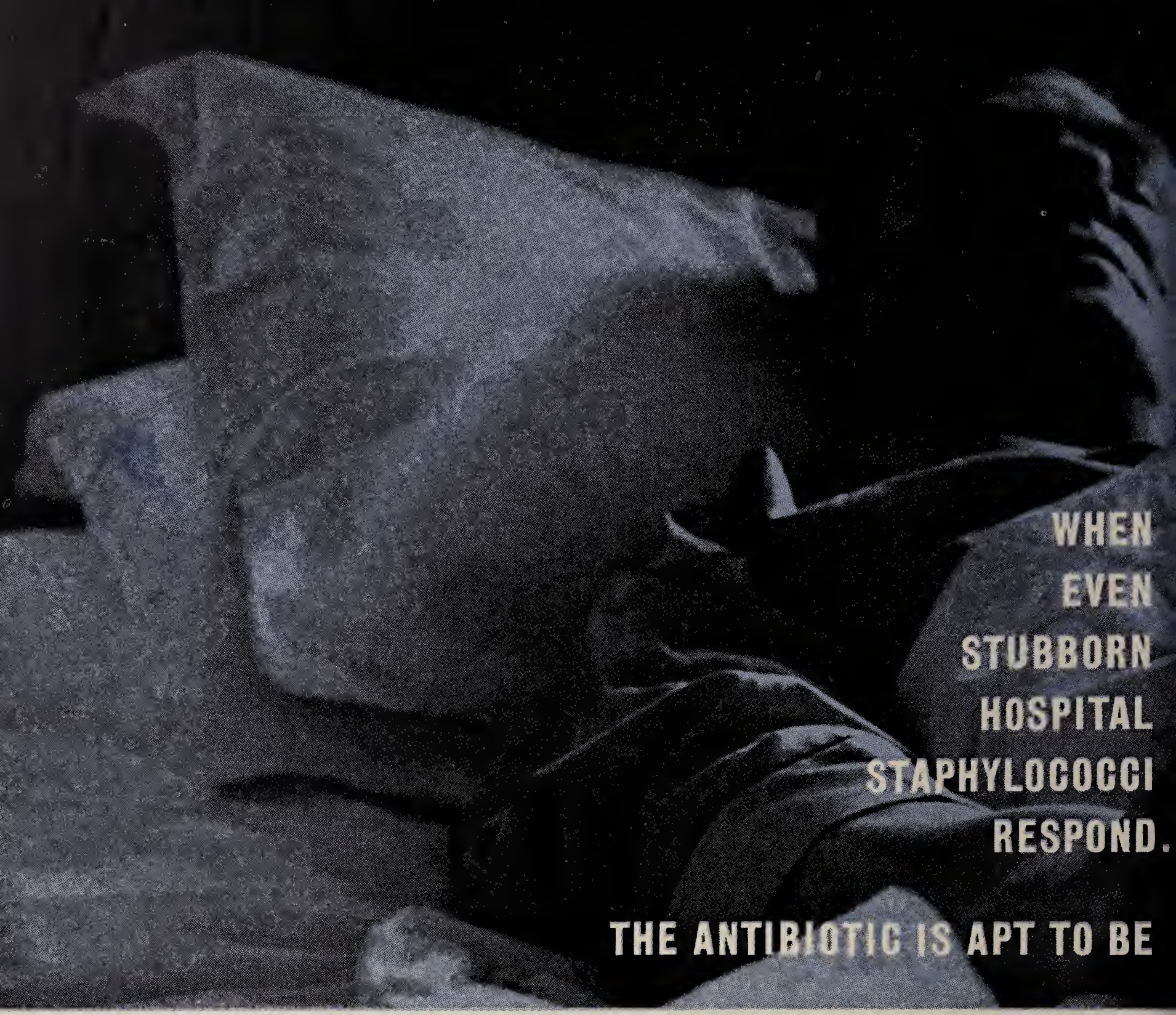

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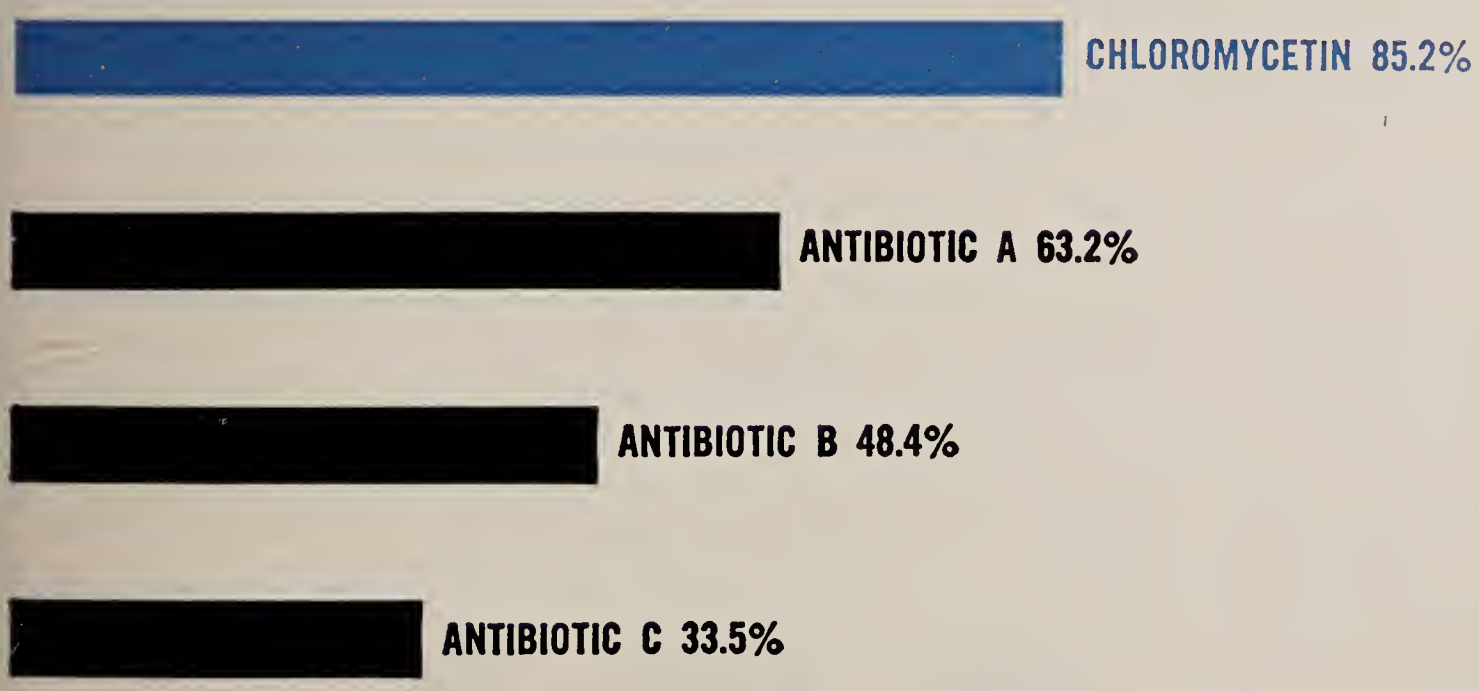

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EDITORIAL

If Winter Comes . . .

Winter is upon us. As we recuperate from the Christmas holidays it is hard to realize that the school year is already half over, and that spring lies only a few weeks away. In many ways, spring is the most pleasant of seasons, a time of sports cars, warm days and short shorts, a season to be enjoyed. But for the 840 medical students at the University of Toronto, spring is a time of gloom and despair, of panic and crisis, for it brings with it the final examinations.

Of all the stresses of medical school, none can hope to match that imposed by the finals. Here the efforts of the academic year become crystallized into one agonizing, six-day endurance test, designed, it would seem, to wreck the most stable body and mind. For many, the exams mean too many cigarettes, too much coffee, and too little sleep. For others they mean amphetamines and phenobarbital, anorexia, nausea, and diarrhoea. For all they mean a month or more of grinding away at the books, when the mind can absorb only as much as the rear can endure. The mental changes which the strain of examinations produce are even more appalling, and sometimes ludicrous. We have all seen them—the compulsives who grow beards to ward off the inevitable, the spastic hypomanics with their hysterical laughs, the neurasthenics seeking escape in sleep, the latent hysteroids assuring each other they are going to fail (especially prevalent among "A" students), and, of course, the dime-a-dozen anxiety reactions.

Balanced against this rather grim spectacle we have the oft-repeated platitudes of those who have gone before, and passed. There are those who would have us believe that the evening prior to an exam should be spent relaxing with a good novel, followed by at least ten hours sleep. We are told that no studying should be done during the week of exams, on the theory that, if we don't know it now, we never will. We have been assured innumerable times that "cramming" is useless; that if we are well prepared, we will have no difficulty.

It is fair to say that there is something wrong, when such a discrepancy exists between what *should* happen, and what *does* happen to those who write examinations. Those who set the exams blame the student's plight entirely on his own slack ways. This is to a large extent true, but it is not the whole story. In the first place, the student does not exist who can recall, without cramming during the week of examinations, the multitude of details which overburden most of our courses. In the second place, pass or fail, every student is exposed to his fellows in that annual House Organ, the Class List, with its diabolical persuader, class standing. And so, in spite of knowing better, we continue to plug in the dying moments of the big push, whether we are scraping for a pass, or gunning for an A.

Final exams, like death and taxes, are here to stay. In their present form they are a fine test of stamina, a fair test of knowledge, and a questionable test of ability (as compared to spot quizzes and all-day orals—God forbid!). In their present form they are a terrific strain, but they need not be so. We offer three suggestions here, all of them controversial, which would go a long way toward relieving the burden which the finals impose. First, give us a week officially (or even two), before the exams in which we can organize and categorize the masses of knowledge we have acquired over the year. Second, split the exams up, so that we write two days, and then have a day's break. Even better, have two papers

prior to the weekend before the exams, and spread the other three or four over the next week. Lastly, eliminate the class list, and inform each student privately of his standing; have him work to better his marks, instead of his classmates.

L.E.D.

Medical Research at the University of Toronto

This feature is continued this month with a report of the activities of the Department of Pharmacology. This report was compiled by R. O. Davies, Ph.D., 6T2. John Mogan 6T1 was in part instrumental in causing it to appear in this issue. There was to be a report from the Department of Biochemistry but our correspondent failed to produce one for us. It is hoped that such a report may be published at a later date along with an account of some of the clinical research.

THE SOCIOPATHIC PERSONALITY

JAMES R. ALLEN, 6T1 &
ROBERT J. McCALDON, 6T0

"Chaque jour vers l'enfer nous descendons d'un pas."[1]

The demands and expectations of society, codified as laws and crystallized as customs, impose on the actions of most individuals a deceptive homogeneity. However, in each group, there are some that are unable or unwilling to accept the standards of their cultural milieu.

Formal psychiatric recognition of these people began in 1835 when Prichard described patients with emotional and volitional defects, a disorder he defined by the terms "moral insanity" and "moral imbecility".[2]

The term "psychopathic personality" perhaps originated with Koch's description in 1891 of a group of peculiarities then fitting into no known class of mental disorder, and yet which was not considered normal.[3] Thereby armed, a great number of workers attacked the problem of the social deviants by classifying them according to their symptoms. Adolph Meyer then showed that some of these were really psychoneurotics, and left us with a group, some of which we now call psychopathic.[4]

This led to the question of the relationship of the psychopath to the neurotic and psychotic—a question answered by some by considering the behaviour of the psychopath as an expression of unconscious conflict, expressed not symbolically as seen in the neurotic, but in socially inept and hostile behaviour.[5] Others coined the term "sociopath" to distinguish the social deviant from the neurotic.

Consequently today, the term "sociopath," or "psychopath" has come to be a vague diagnostic entity embracing a wide variety of behavioral disorders[6] and the numerous classifications of types, often smacking more of accusation than description, are drawn on those sands that are washed by the waves of uncertainty and confusion. However, they do form a very real group whose main characteristic is suggested by the name "sociopathic personality", a pathological lack of conformity with the values of their society.

As they saunter, reel and plunge along their varied paths of social maladjustment, the psychopaths form a parade of contradiction. They are said to be aggressive and rebellious, and yet to be passively submissive; to be emotionally shallow and superficial, and yet to be as dependent as a child on its parents; to be impulsive and aimless, yet to be cunning and sly; to be unable to learn by experience, and yet to form an important portion of the scholarly and creative pride of our civilization.

In biosocial development we learn passively to accept the framework of permissions and taboos of our culture, and actively to suppress overt hostility and aggression, and to accept increasing responsibility toward others. Here lie two great highways to social deviation; failure in social participation, or failure to participate in a manner which is culturally acceptable.

Cleckley postulates a "serious subtle disorder at deep levels, disturbing the integration and normal appreciation of experience" in the psychopath.[7] This "semantic disorder" appears substantiated by the experiments of Simon, Holzberg and Unger, who found that, in response to a multiple choice test, a group of female psychopaths showed indications of much better judgement than to the same items presented in the form of a completion test. This "would imply that the psychopath has learned social values and is able to recognize them

when they are overtly presented (multiple choice) but when the psychopath is thrown on her own resources in resolving a conflictual situation (completion test), these learned values are not readily available as guides, apparently because of their superficial incorporation into the personality structure."[8]

Incidence

The difficulty in deciding the incidence of this disorder is bipartite: the category has become a nosological waste-basket, and at some times in our lives, social deviation is included in the behavioral repertoire of us all. However, it is said to account for 5% of all military neuropsychiatric disorders (Carron), 26% of admissions to U.S. Veterans Hospitals, and 19% of Sing-Sing prisoners (Guleck).[9] These are, however, only the unsuccessful social deviants; under certain circumstances, groups may tolerate or even reward behaviour others regard as deviant. Among the Dobu natives, "the good man, the successful man, is he who has cheated another of his place."[10]

Aetiology

A. organic

Lovett-Doust, in a study of psychopaths in prisons, found evidence of constitutional immaturity as revealed by the technique of capillary microscopy.

Silverman found that 48.4% have an abnormal EEG. Cohn found that, as a group, psychopaths have a 2½-fold greater frequency of abnormal EEG patterns, some characterized by slow occipital-parietal waves reminiscent of tracings of the pre-adolescent.

Endocrine imbalances have been suggested, for often there appears to be spontaneous remission in middle age.[9]

B. environmental

Here two factors are important; the parent-child relationship, and the reaction of others to the social deviant.

I. *Parent-Child Relationship*

(a) The over-protecting, indulgent mother accepts overt hostility and aggression, thus encouraging delay in biosocial maturity and consequent distortion in subsequent development or encouraging dependency and inadequacy.

(b) Rejection encourages shallow emotional development and attention-seeking, ingratiating behaviour, or open hostility to the whole of society.

(c) Vacillation in parental attitudes leads to disdain towards authority and the easy shifting of outward attitudes for the purpose of manipulating others.

II. *The Reactions of Others*

The reactions of associates may be an antidote to the tragic triad in parent-child relationships, for from the reactions of others we are said to develop our evaluation of ourselves, and if we lack this, self-control is learned with difficulty, if at all. Society is largely apathetic or disdainful to the obnoxious young sociopaths and shuns them, leaving them devoid of this stabilizing influence. Hence the psychopath is frequently said to be without conscience and without guilt.

C. heredity

Sociopathic parents are said to have similar offspring, but the evidence of a genetic factor is far from conclusive.[9]

Psychopathology

On referring to the great number of varying definitions and classifications of the sociopath, one finds a medusa of traits. Yet this seemingly nebulous sickness may be found to have certain definite thought patterns and behavioral characteristics. There is dysfunction here in all three compartments of thinking, feeling, and behaviour. The sociopaths are further complicated by a warped self-concept (ego), a vacillating set of motivations (conation) and a weak or absent conscience (superego). Unlike the schizophrenic, their pathology may be masked by the superficial appearance of normalcy. The degree of social devia-

tion is recognized not by a single examination of the person, but by the overwhelming history of repeated scrapes, misdemeanours and inept behaviour.

These ill people often do not appear sick, but rather senselessly wicked. They are rarely involved in major crimes; they do not have the persistence in attaining the goals of the master criminal. They make little attempt to conceal their misdemeanours, hence are often caught. But only 19% of convicted criminals are true psychopaths.[9] Criminal convictions are rare for two reasons. Their activities often involve minor, unpremeditated nuisance crimes, making their authors appear merely full of boyish exuberance —the full-grown cavaliers. Also, they possess the remarkable ability of superficial rationalization; they can convincingly persuade almost anyone who will listen that it was not really their fault, that there are a million reasons why *anyone* in the same set of circumstances would have acted in the same way.

Women are especially prone to be mesmerized by the psychopath's debonair charm, small boy's irresponsibility and grandiosity. Cleckley proposes that it is the woman's maternal instinct that the psychopath arouses; she will learn too late that here is a small child who will never grow up, despite her tender care. He suggests that male psychopaths are seldom as virile as the average man.[7]

Only a small percentage of sex offenders are sociopaths, yet they often become involved in sexual aberrations. This is due to a characteristic amorphous sexuality. "Self-gratification" is a key word of sociopathology, and they will achieve this by any methods available at the moment, yet rarely do they persist in one form of perversion exclusively. In the sexual sphere as well as the other phases of their existence, psychopaths are governed by unpremeditated, almost reflex, thoughts and deeds.[11]

The sociopath has a normal level of intelligence, but his work and scholastic record are frequently marred by outbursts of anti-social behaviour. There is a definite tendency to habituation to alcohol, drugs, and gambling. The outcast who indulges in these and then pursues bizarre crimes, the example of depravity so willingly described by the "reformers" is frequently the psychopath. With characteristic lack of concern and insight, he looks for his kicks and succeeds in adding to the social problem his abnormal character has already created.

He suffers from a "Hedonistic overbalance" and marked egocentricity.[9] Far from being a masochist, he detests punishment, despite the fact that his actions often hurt himself as much as others.

With the unfortunate hindsight often exhibited by workers in the field of human behaviour, there have been described increases in enuresis, nail-biting, temper tantrums and sleep-walking in children who later become sociopaths.[9] These traits, however, are found in the history of other illnesses and hence are of little significance in themselves. It is important, however, to recognize their cause, and if disturbed parent-child relationship is implicated, to suspect early sociopathy.

Literature is replete with characters possessing definite sociopathic traits. Edmund in "King Lear", Iago in "Othello", Heathcliffe in "Wuthering Heights", Scarlett O'Hara in "Gone With the Wind", the two children in "The Turn of the Screw", the eldest Karamazov in "The Brothers Karamazov", Deborah in "No False Vision" and the teenage hero in "Rebel Without Cause" are a few examples.

Famous psychopaths include Dostoevski, Swinburn, Baudelaire, Richard Wagner, Jonathan Swift, Paul Verlaine, Lawrence of Arabia, Jack the Ripper, various members of the Beat Generation and that old prototype who has been the source of inspiration to many of his ensuing confreres, the Marquis de Sade. Ruth Benedict has described a whole

culture of people which our society might call psychopathic—the Dobu.[10]

Perhaps the most exasperating facet of the disordered character is that he does not appear sick, and so, rarely ends up in medical hands. In the minds of society, as Aubert has said, "The sick suffer, the evil do not."[16] The psychopath, with his lack of concern or insight and his plausibility and ability to avoid punishment, seems to be childishly happy in living his twisted life, but this superficial happiness merely masks his deep-rooted pathology. He never seeks medical help on his own, and rarely is treated by the psychiatrist, unless he is referred for study by the courts. However, if one looks deeper into this person as a patient, one often finds that he is hounded by uncontrollable thoughts; his decisions are made wholly without concern for the consequences. His actions may be looked upon as an unconscious, uninhibited compensation for that which was denied him in childhood.[11] At any rate, he is mentally ill, and this fact is poorly recognized both by the medical and the legal profession; but most poorly of all by society. The impulsive may go to a lawyer and the inept may go to a doctor, but the inadequate go unobserved.

Treatment

Adequate treatment is hampered by late diagnosis, poorly understood psychodynamics, legal problems and general lack of comprehension about the illness. The patient's lack of concern or insight adds to the difficulty.

Electro-convulsive therapy and various drug treatments have been tried without success. Frontal lobotomy has been used as a last resort in severe, unmanagable sociopaths. It has made a few more tractable, and has markedly dispelled the last remnants of self-control in others.

Prison, of course, provides no answer. It keeps the psychopath away from society for a time, but he usually emerges worse than before. The idea that the psychopath cannot learn is false. In prison he manages to absorb a great variety of anti-social traits, deeds and companions. He will become stamped with the sex patterns of such institutions[12] and this will add to his social problem. His misdemeanours are usually so minor that the prison cannot keep him long enough to wait for the spontaneous remission which seems to come with middle age.

It has been suggested that, where minor sociopathic traits exist, the firm control of a wife or husband may help to keep the individual out of trouble. This is a wearying task for even the strongest nursemaid and is further complicated by the fact that psychopaths have a tendency to marry psychopaths.[13]

Recent attempts to help these people by psychotherapy on an out-patient basis have proved inadequate. They make a convincing superficial adjustment but gain no real insight into their problems, as they return to their old behaviour pattern once out of the therapist's office.

The present Ontario Hospitals are not equipped to handle sociopaths. A few end up there showing behaviour bizarre enough to be certifiably mentally ill. Others are referred from the courts to be cured of drug addiction. Valiant attempts are made at psychotherapy aimed at re-habilitation. Much time is spent with these sociopaths because they are a source of nuisance on the wards and demand constant attention, and because they are often charming and fascinating. The realistic psychiatrist is too wise to think that he has cured these people when they are discharged, but he hastens to send them back into society to make room in the hospital for patients that he *can* help. A sociopath retained against his will succeeds in disrupting other patients and staff to such a degree that acute psychotic and neurotic reactions may be precipitated. Yet certain selected patients exhibiting antisocial behaviour, many of whom are later diagnosed as sociopaths, are admitted,

studied, and subjected to therapy in the Ontario Hospitals. Although facilities are not yet available for the adequate treatment of this type of illness, steps are being taken towards its understanding. However, as far as therapy is concerned, both the hospitals and the prisons have largely failed.

Two dramatic experiments are going on at present; one in the United States, the other in England. These may provide some of the answers.

On an island in the East River near New York rests Riverside Hospital. This one hundred and forty bed hospital is devoted exclusively to the treatment of adolescent drug addicts, 65% of whom are definite psychopaths. Patients are confined there by legislation under the Public Health Act (not the Criminal Code), an admission that such a problem is an illness, and they may be retained up to three years. The staff outnumbers the patients almost three to one, allowing a close, personal supervision at all hours of the patients' daily lives. Some good results have been obtained; statistics are not yet available.[14]

A similar project is underway in the Social Rehabilitation Unit of the Belmont Hospital in England. This unit has one hundred beds and is solely for the treatment of young psychopaths. It has been in operation for seven years. Here, also, there is close staff-patient contact and some excellent results are reported. The process is described as "an intense socializing experience."[9]

These institutions are precisely what Cleckley advocated be done to treat the psychopath in his classical study, "The Mask of Sanity."[7] In prisons sociopaths have proven that they can learn. If they are completely cut off from their previous associations and intensively re-socialized, they may discover how to live in society.

Prophylaxis

There is hope in this sphere as well. We know that infant rejection, disturbed parent-child relationships and emotional poverty are important in the aetiology of the condition. Social groups and the Children's Aid Society are already helping to improve such strained environments, especially in the care of institutionalized children in those deprived of the physical necessities of life. Unfortunately, little is being done to ameliorate the situation of children who are well cared for physically but who are emotionally deprived. The medical practitioner is the person who should be most able to spot early tensions and their symptoms, and do something about them. In some cases, discussing the problem with the parents may be enough. In others, prolonged psychiatric management may be warranted. Social agencies could be beneficial in such work, aiding in early diagnosis, treatment and public education.

Prognosis

At present, the prognosis for the full-grown "moral defective" is gloomy. There often is a "spontaneous remission" in middle-age.[9] However, it is doubtful whether such people have really improved their pattern of living, or have merely learned to manipulate other individuals enough so that they achieve their own ends without the friction encountered in the callowness of youth.

Some improvement with psychotherapy has been encountered when the patient shows a certain amount of insight and remorse. But these are rare qualities in a definite sociopath. Some can recognize that they are different from the rest of society, and may feel their own worthlessness. Baudelaire was so acutely aware of this that he abandoned himself in prayers to Satan.[1] However, this is not true insight or remorse, as the sociopath often revels secretly in his misdeeds. Sade writes in the words of the giant Minsky, "Nature has given me the taste and ability for all crimes."[15]

This is the too-common attitude of the sociopath. There is no guilt; this is simply the way things are with him and he defies anyone to change him.

Hope for this lugubrious situation lies in prophylaxis, early diagnosis, and possibly in institutions such as the two described. Fotheringham recommends that the patient be "made to face the consequence of his action in a non-punitive atmosphere."Cleckley strongly advocates separate hospitals for psychopaths where they could be legally retained once the diagnosis is made, whether they had committed a major crime or not. They would not be released until it was felt that they were completely rehabilitated.[7]

Much more may be accomplished if this illness is regarded as an illness. Many lawyers as well as psychiatrists recognize that the McNaghten Rule for assessing responsibility for criminal actions is archaic. And yet it stands, making the sociopath, following the dictates of his overwhelming impulses, as responsible as a well person. Is the psychopath, with his infantile conscience, any more guilty than the paranoid schizophrenic following his delusions? Few of us are in a position to change the law, but it is a moral question which we ought to consider.

Summary

The character disorder creates problems in many spheres for many people. It is not yet completely understood, not yet well-treated. However, something is being done. If the medical profession refuses to give up in despair and attempts to treat the condition vigorously, this most difficult of all psychiatric problems may, in the future, be better defined, better understood and better treated.

Acknowledgement

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THE DISCOVERY OF MEDICAL HYPNOTISM – A HISTORICAL REVIEW

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GENERALLY, the practice of hypnosis is said to date from Mesmer in the late 18th Century. However, when one considers that in Ancient Greece there were temples constructed to Aesculapius, the God of Healing, in which it is said, the priests put people into a sleep-like state called the "temple sleep" or incubation during which healing suggestions were given, one can imagine the probable very early use of hypnosis. There seems sufficient evidence that Druids in England also produced a similar state. Hinduism and Buddhism have taught for centuries, methods of mental concentration and physical exercises producing altered states of consciousness, which may be considered forms of self-hypnosis, further indicating its early widespread use.

Franz Anton Mesmer (1734–1815) began studies in theology and philosophy at Vienna then graduated in Medicine in 1766. He published a book a few years later which proposed the so-called "animal-fluidistic-magnetic" theory of suggestion therapy. Part of his technique of induction included the placing of his hands upon the shoulders of the patient, then stroking the arms downwards to the fingers. He also made various "magnetic" passes and gentle, soothing contacts with his hand over the patient's forehead. Mesmerism, as it had been termed, was not acceptable because of the theory and there was immediate objection to his principles. The French Academy of Sciences forbade its use in France. However, physicians in Russia and Denmark were allowed to practise it and Mesmer subsequently became a lecturer of the Prussian Academy.

The battle for establishment of hypnosis continued in the 19th Century. Elliotson, a brilliant physician in the early part of that century in England, made a significant contribution to medicine with the introduction of the stethoscope, an instrument originally devised by Laennec. He also did considerable research in hypnotism, and in 1846 chose hypnosis as a subject for the Harvey Oration. For this, he was soundly condemned by the Lancet, and he promptly lost his professorship at a London teaching hospital. In contrast, Esdaille established a hospital in India under protection of the British government, for the express purposes of applying hypnosis in medical and surgical cases. On the continent, such men as Charcot, Liebeault, Babinski, Bernheim, Heidenhain and Forel were quite interested in its use and application to medicine. Freud's research in Breuer's work on recall and regression side-tracked his interest to hypnosis, which he subsequently used to explore the cause of symptoms in his neurotic patients. Not much later he dropped the term hypnosis in favour of "free-association", the psycho-analytical method which developed from his previous use of the hypnotic trance.

It was, however, a Scotsman's perseverance which established the use of hypnotism in medical practice. James Braid, born in 1795, had at the age of 20 years received his M.R.C.S. from the University of Edinburgh. It was not until the mid-nineteenth century that he became interested in hypnotism. Ch. Lafontaine from Switzerland was travelling about the continent at that time lecturing, demonstrating, and "curing" with Mesmerism. In 1841 Lafontaine lectured in Manchester. Immediately after this occasion, Braid organized lectures and demonstrations in order to disprove the existence of "magnetism". This led James Braid to the discovery and practice of bradism which he later termed "hypnotism".

In order to disprove the "animal-magnetic-fluidistic-mystic" theory of Mesmer as demonstrated by Lafontaine, Braid experimented at home with his wife and servants, finally developing a simple method of inducing hypnotic trance. This involved fixation of the subject's eyes on

a bright external object, then fixation of the subject's mind on ideas concerning the external object, with gentle but firm suggestions of relaxation and sleep. With this technique, he was able to prove the "magnetic" passes in Mesmerism were not required.

His theories and lectures were received with scepticism and contempt. He was accused of immorality, irreverence and of depriving subjects of their free will. In fact, it was in a reply to a crushing sermon by Rev. McNeill, St. Judes, Liverpool, that Braid laid the corner-stone of medical hypnosis. In this published and advertised reply, Braid explained his method, uses and theory of hypnotism. His was the first scientific evaluation of the psychological value of hypnosis in medical therapy. At the same time, it is interesting to note that he disclaimed it as a universal remedy, yet claimed that hypnosis was a necessary adjunct to medical therapy, "provided it is applied in the required professional way; it ought not to be the toy of the uninitiated or of the quack".

Thus the corner-stone was laid, yet the building is still incomplete. Hypnosis has enjoyed periodic revivals since the time of Braid but it is still unacceptable to most practitioners of medicine. Little is known of the nature of hypnosis. All of the published theories and concepts are unacceptable. We know certain techniques can induce a state of increased suggestibility associated with certain physiological phenomena, but no satisfactory unifying hypothesis has yet been evolved.

"Hypnotism is a psychic process by which a mental representation of psycho-sensorial perception of a certain idea, feeling or impulse, is introduced and accepted without much prejudice or psycho-analytical resistance by our mind, by means of certain methods and dialectics." Can we accept this definition? Surely, further neurophysiological and psychological research can produce a better basis for its use. Professional scepticism and distrust is due to this lack of explanation and to its wide use by charlatans and public performers. One can readily see why the British parliament passed the Hypnotism Act (1953) controlling its use by stage performers, and why the Church gives opposition to the use of hypnotism.

In 1955, a subcommittee of the British Medical Association defined the hypnotic state as "A temporary condition of altered attention in the subject which may be induced by another person, and in which a variety of phenomena may appear spontaneously, or in response to verbal or other stimuli. These phenomena include alterations in consciousness and memory, increased susceptibility to suggestion, and the production in the subject of responses and ideas unfamiliar to him in his usual state of mind. Further phenomena such as anaesthesia, paralysis and rigidity of muscles, and vasomotor changes can be produced and removed in the hypnotic state."

In a further published statement, this subcommittee has opened the field of research for the development of hypnosis, which has remained relatively dormant from the time of Braid over a century ago. "Hypnotism is of value and may be the treatment of choice in some cases of so-called psychosomatic disorders and psychoneuroses. It may also be of value for revealing unrecognized motives and conflicts in such conditions. As a method of treatment, in the opinion of the subcommittee, it has proved its ability to remove symptoms and to alter morbid habits of thought and behaviour. The subcommittee therefore regards hypnotism as a proper subject for inquiry by the tried methods of medical research."

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HYPNOSIS: THERAPEUTIC TOOL OF THE GENERAL PRACTITIONER

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IS hypnosis a therapeutic tool which the general medical practitioner should feel free to use? Some feel that hypnosis should be used only by a fully qualified psychiatric specialist. Others believe that hypnosis lends itself to the general practice of medicine naturally and with necessity.

The consequences of the answer to this question have a far reaching effect in medical education. Assuming that medical school and internship constitute the basic training of the general practitioner, and if it be decided that hypnosis is a procedure to be used by him, then gaining a knowledge of its indications, contraindications and technical methods of administration, should be as much a part of undergraduate medical education as a similar knowledge of insulin. The question can be discussed on the basis of:

a) The dangers surrounding the use of medical hypnosis.

b) The therapeutic indications for the use of hypnosis.

c) The practicality of hypnosis in general practice.

Dangers

The commonly quoted dangers of hypnosis are as follows:

(i) The danger of loss of professional status in the eyes of the patient. It has been pointed out that the general practitioner must be aware of the social setting of his practice. He may develop the impression of witch-doctoring and mysticism by the use of hypnosis with his patients. He may embarrass both the patient and himself. Watt[1] feels that looking deeply into the eyes of a patient while telling him he is feeling sleepy, makes the doctor look ludicrous. Thus he loses rapport with his patient. Such an objection is valid only in as much as the operator fails to make the true nature of hypnosis clear to the patient. The general practitioner should be in a better position to teach his patients correct concepts concerning hypnosis than the already somewhat mystical psychiatrist.

(ii) The danger of improper motives on the part of the physician may lead to the use of hypnosis in non-indicated situations. Mason[1] lists three of these improper motives: First, those of the frank charlatan; second, those of the enthusiast who constantly sees new cures and applies them with great fervour; and finally, those of the professional failure who uses hypnosis to give himself a sense of power and grandiosity which compensates for his inadequacy. The general practitioner must be very sure of his motives, and always be sure that this method is not only indicated, but also is being used solely for the benefit of the patient and not for personal gain.

(iii) The danger of the patient not awakening from the trance is frequently mentioned. This rarely occurs. When it does, it is the result of two easily corrected attitudes. The patient may feel completely comfortable in the trance state and not want to be disturbed. This is overcome by firmer suggestions of awakening. Inability to awaken a patient may be the result of resentment of the operator for being demanding rather than suggestive. This is usually overcome by calmly discussing the reason for resentment with the fully conscious but hypnotized patient. At worst all patients in trances, when left to themselves, without exception fall into natural sleep and waken physiologically.

(iv) Associated with the above danger it is often argued that in the disturbed patient a latent psychosis may be precipitated. First, let it be said that in the patient with a deeply rooted problem or latent psychosis, the hypnotic state is rarely reached. If it is induced, the hyp-

nosis rarely reaches the level at which the psychopathology is functioning. Mason, in his psychiatric practice had three psychotic episodes following the use of hypnosis in over 300 cases during a four year period. This was no greater an incidence than that found following any other method of psychotherapy. Kennedy[2] concludes: "It is, on the whole, a method which leaves few scars and makes no fundamental change in the personality that would not have occurred in the course of individual development." Providing the general practitioner has a sound working knowledge of hypnosis he has little to fear concerning the psychological consequences of its use.

(v) The development of a pathological dependence on the doctor or on hypnosis, is suggested as a danger. It is agreed that a dependency may develop, but this is no deeper than that which may develop and is accepted during psychotherapy. In hypnosis the dependency can be effectively removed by post-hypnotic suggestion. It must be recognised that all therapy induces dependency whether it be for hypnosis or little white heart pills.

(vi) Removing symptoms without discovering the underlying organic or psychological cause is an obvious and real danger. However, it is not peculiar to hypnotic therapy, but is inherent in all symptomatic treatment. If, after thorough investigation and the necessary consultations, the cause has not been elucidated, the general practitioner should feel free to institute symptomatic therapy including hypnosis, where indicated. It is better to treat a patient symptomatically with a resulting happier patient than to leave him with no treatment at all.

From the above it is apparent that a psychiatric specialist's training and knowledge are not needed to fully avoid these dangers.

Indications

In every illness there is a psychic and an organic component. For proper therapy both components must be treated. In certain diseases treated by the general practitioner the psychic component is best relieved by hypnosis.

Before hypnosis is used the following conditions must be fulfilled:

(i) A more efficient medical treatment whereby a cure or symptomatic relief may be obtained must not be available.

(ii) The cause of the disease, be it organic or psychological, should be known. However in undiagnosed cases of suspected psychological cause hypnosis may be used as an investigative method.

(iii) The patient must understand the nature of the hypnotic treatment and be completely willing to co-operate.

The absolute indications for hypnosis are few. In general practice any severe pain of expected long duration that is unrelieved by drugs is an indication. This includes the pain of terminal malignant disease, the pruritis of jaundice and the severely distressing symptoms of diseases for which there is no remedy, such as essential dysmenorrhoea.

Hypnosis is indicated where the anxiety component of organic illness becomes more disabling than the primary disease. A common well-known example of this is the cardiac neurotic, more crippled by anxiety than by his heart.

Hypnosis may be useful as an "umbrella" under which other medical therapy may be carried out. Suggestions are made to reduce discomfort and anxiety which normally might make the patient interfere or refuse to carry on with his medical therapy. The burned patient, the patient receiving physical therapy, and the patient with dermatitis are good examples. In this latter case the itch-scratch reflex may be broken by suggestion, allowing healing to occur.

As an investigative measure in the hands of the general practitioner, hypnosis is limited in scope. It is useful to the physician in mild neurotic and psy-

chosomatic disease, where, by direct questioning of the patient in the trance state he may be able to give a clue as to the basis of his trouble. In this type of disease the pathological subconscious feelings may be repressed by conscious anxiety. The trance allows the repressed feelings to be more easily expressed than in the non-hypnotic state.

The relief of anxiety is the main indication which the practitioner will find for hypnosis. Often this will involve teaching patients to relax by self-hypnosis. The typical candidate for such therapy is the ulcer-prone, worried, tense, executive. A ten minute self-induced trance allowing complete relaxation with post-hypnotic suggestions of vitality will in many instances provide more relief from anxiety-produced tensions and their organic components than the potentially addicting sedatives. In obstetrics the use of self-hypnosis, learned prenatally, can relieve tension-produced pain during labour, often obviating the use of analgesics with the accompanying fetal respiratory depression. Organic symptoms produced by deeply rooted anxiety often are necessary for the maintenance of psychic equilibrium. As such they can rarely be removed and if they are, new symptoms spring up to take their place. In cases where the necessary symptom is disabling, time distortion by hypnosis may allow the patient to experience several days of symptoms in a short span of time. The patient is taught self-hypnosis and when the symptom begins he enters the trance state in order to experience the next few days during a short period. Having derived the necessary psychic benefit of his symptoms he is then free to carry on symptom-free for the next few days. It must be realized that symptoms of basic personality disturbances such as established hysterical conversions, obsessive-compulsive neurosis, alcoholic addiction and sexual perversion are usually completely refractory to hypnotic therapy.

It has been shown that, in general medical practice, indications for hypnosis do arise and that the practitioner is capable of recognizing these indications.

Practicality in General Practice

In presenting their arguments against the use of hypnosis by general practitioners, psychiatrists cite its dangers and the difficulty of determining when it is therapeutically indicated. However, the common excuse of the general practitioner for avoiding its use is the actual impracticability of hypnosis. Factors in this alleged impracticability are as follows:

(i) It is generally thought that extensive training of the operator is needed not only in methods of hypnosis but also in psycho- and hypno-analysis. It does not, in fact, require vast amounts of time to gain a workable knowledge of the concepts and technicalities of therapeutic hypnosis as used in general practice. At present three-day courses are available to general practitioners giving them a basic knowledge and method on which to build. In medical school a series of eight lectures and four clinic periods would probably equal this. Junior internship would provide opportunity for practice under supervision just as it does for other procedures.

(ii) Hypnosis is one of the most expensive therapeutic tools available today because it involves large amounts of professional time. Steward[1] averaged about eight to ten weekly visits involving thirty to fifty minutes per visit in a series of patients treated by hypnosis. If a general practitioner's office time is worth twenty dollars an hour, the expense of such treatment can be seen. Thus hypnosis is practical only when results can be achieved quickly or else when the severity of symptoms make it worthwhile.

It has been said that hypnosis is not practical as the conditions in which it does work are just as amenable to other, more efficient, recognized forms of medical therapy. However, this is only partially true. When it is true certainly hypnosis should not be used, but where

patients are suffering from severe crippling symptoms unrelieved by the best medical treatment then hypnosis becomes practical.

(iii) The percentage of patients that are able to enter the trance state is an important practical consideration. The literature is almost unanimous in placing the figure at about ninety per cent of all patients.

(iv) It is still believed by many[3] that the operator must have certain physical and psychological attributes. It will become apparent in the remainder of this article that this is not so, any more than it is for the physician.

In the hands of the general practitioner, adequately trained in its induction, ready to deal with difficulties as they arise, and with a practical knowledge of how to use the trance state, it has been shown that the dangers to the patient of hypnosis are almost non-existent. It is also apparent from the foregoing that the alert general practitioner will invariably come across and recognize definite indications for hypnosis within his practice. Finally it has been pointed out that hypnosis when properly applied is practical and economical for both doctor and patient.

Method of Inducing Hypnotic Trance

Having shown that those of us who will be in general practice should include this as a specific method of treatment in our "little black bags" of therapies, a short summary about the technicalities of hypnosis is in order. Perhaps this will uncloak the mysticism sufficiently to give the faint of heart adequate impetus to study the subject further, and actually make use of it therapeutically.

Rowsell[4] has outlined the following method of hypnotic induction:

(i) The operator must know what hypnosis is and even more important what it is not (most doctors do not know). Hypnosis is not a prestige method of symptom removal. It is not the power of one person over another. It does not render the patient unconscious or destroy his will power. It does not prevent liars from lying or make the patient reveal personal secrets against his will. Deception causes the patient to wake up. Hypnosis is not someone doing something to someone else. It is a "learning session." It is a human relationship in which one person accepts or rejects the suggestions or signals of the other. Hypnosis is a deliberate attempt of the patient to reach a trance state at the direction of the operator. It is a learned process by which the patient, receiving signals from the operator, exercises the imagination. This produces a frame of mind in which suggestions, if agreeable, are accepted as a type of reality, and yet the patient remains fully conscious of the fact that he is in the hypnotic state. From this it can be seen that the doctor need have no fear of failure of induction, as hypnosis depends primarily on how well the patient has learned the process.

(ii) The patient must be fully informed and oriented as to the nature of hypnosis or "suggestive relaxation".

(iii) The patient must be fully relaxed, lying or sitting in a comfortable atmosphere, free of annoying or distracting sensory influences.

(iv) The patient next excludes external visual stimuli and reduces conscious cerebral activity to a minimum by fixing the eye on some point.

(v) Repetitive auditory stimuli are then begun in the form of suggestions given in a modulated voice indicating calm and confidence. These suggestions are repeated at ten second intervals.

(vi) The patient enters the trance state which is indicated by glazing of the eyes, fluttering of the eye lids and deep regular breathing. Depending on the nature and will of the patient the trance may be deepened from a light trance, through a medium trance, to, in a quarter of the cases, a deep somnolent trance. Light trance is indicated usually by eye closure and allows skin anaesthesias to

be suggested. In medium trance the pulse slows and though there may be some amnesia following the trance, during it the patient is conscious. Hallucinatory experiences may be induced at this time. In deep trance the patient's eyes may be open and motor activity may be normal as in a sleep-walker. It is possible for there to be complete amnesia for the trance in this stage. When the patient has reached the desired stage therapeutic suggestion may be begun.

Nature of Hypnotic Suggestions

(i) The suggestions must never be given as orders. Such prefixes as "You can imagine", "You might be interested to—", or "Would you like to—" make orders into suggestions. This allows the patient to decide whether or not to carry out the suggestion. If a suggestion is rejected the patient remains in trance, but if an order is rejected the patient often awakes, and confidence in the operator is lost. Suggestions also allow the operator a loophole to suggest the opposite in a case such as, "Your hand may be getting lighter". The patient's hand begins to drop because of rejection of the suggestion. The operator has made it possible then to state, "I see your hand is getting heavier". By the use of suggestions the patient's co-operation is insured throughout the trance.

(ii) Suggestions must always be positive in nature, simple, and direct, in that there must be no confusion or conflict in the patient's mind concerning what is suggested.

(iii) Emotional or sensory experiences are the commonest type of suggestions made. During induction feelings of calm, relaxation, drowsiness, heaviness and sleep occur. To take a patient from a light to a deeper trance, suggestions of going "deeper and deeper" are made. Imaginatory situations are suggested in producing therapeutic effects. For instance, an anaesthesia of a hand may be induced by suggesting the patient is dipping the hand in a bowl of ice water, and it is becoming numb.

(iv) Therapeutic suggestions must suggest gradual change, allowing the patient time to incorporate the experience as actually occurring.

(v) Self-hypnosis may be taught by suggesting to the patient that he may follow the steps outlined in the above method and thus enter the trance state. Post-hypnotic suggestions are commonly used to extend the therapeutic effect of the suggestions beyond the trance period. Such a suggestion may be that the patient will feel refreshed and relaxed following the trance.

Conclusion

Whenever a physician treats a patient, whether it be by pills or a pat on the back, he is practicing psychotherapy by his appearance, what he does and what he says. The general practitioner cannot avoid psychotherapy, and thus he should not avoid hypnotherapy when it is indicated. To do so is as great an error as to fail to give a patient adequate sedation for pain. However, he must know many methods of hypnotic induction, how to deal with reversals and the unexpected in the trance and, finally, how to use the trance therapeutically. If hypnosis is to become a therapeutic tool of the general practitioner, the logical place to begin its teaching is in the medical school.

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WILSON'S DISEASE

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Introduction

In 1912 the eminent British neurologist Kinnear Wilson described a group of signs, symptoms and pathological findings which he felt represented a clinical entity. To this day little can be added to improve upon his description of what is now known as Wilson's disease or hepatolenticular degeneration. Prior to Wilson other authors had reported cases which, when reviewed and re-evaluated, appear to represent cases of Wilson's disease.

This disease is a genetically determined condition involving copper and/or protein metabolism. Clinically it is characterized by the triad of nervous system involvement, liver cirrhosis and Kayser-Fleischer rings of the cornea. The clinical manifestations may be mainly neurological or hepatic, or they may be a combination of the two with one form usually predominant. The condition usually presents in the first three decades of life, is progressive and always fatal.

This disease entity is considered to be one of the inborn errors of metabolism. These are genetic defects in which one or more intermediary metabolites accumulate in the organism to such an extent that they may be easily demonstrated in the tissues or urine. Such accumulations are due to the inhibition, overloading or actual deficiency of one or more enzymes. Wilson's disease is one such error.

History

Prior to Wilson, Westphal[2] in 1883 and later Strumpell described a similar condition, the symptoms of which resembled multiple sclerosis but in the absence of plaques of demyelinization it was called pseudosclerosis.

The cirrhosis as a part of this syndrome was overlooked until Spielmeyer reexamined the cases many years later and showed that pseudosclerosis and Wilson's disease were the same disease. The Kayser-Fleischer rings were not described by Wilson in his original description. Kayser first described the corneal ring in 1902 in a case diagnosed as multiple sclerosis but it was Fleischer who appreciated its significance. Haurowitz in 1930 noted a marked increase in the copper content of both liver and brain. In 1948 Mandelbrote[3] and associates observed a high urinary output of copper and noticed that this was increased by the administration of BAL. In the same year Uzman and Denny-Brown found that a persistant aminoaciduria is associated with the disease.

Pathology

The pathological changes are more or less confined to the deposition of large amounts of copper in the liver, brain, cornea and kidney with the liver and brain showing gross damage. There is a greater than normal amount of copper in the other body tissues as well.

Grossly, the picture found in the liver is one of post-necrotic cirrhosis and is not specific for Wilson's disease.

Microscopically, the cells vary in number from a few to many in each liver lobule and the cells themselves[4] vary from those of normal appearance and arrangement to those which are abnormal, shrunken or necrotic.

Uzman[4] has shown by biopsy specimens in early cases, marked irregularity in cell nuclei even in lobules containing no copper. He also noted that the nuclei stained poorly, were vacuolated and that, in some, the chromatin was poorly defined.

On staining, the copper showed as a black precipitate characteristically distributed as perinuclear plaques which in some cases extended toward the periphery of the cell where it was less dense.

At no time was copper detected in the Kupffer cells, even in lobules undergoing obvious necrosis, and in no case was there evidence of inflammatory disease.[1]

On gross examination of the brain the main lesion found was cavitation of the lenticular nucleus, the severity varying with the duration of the disease. The area of destruction involves the putamen and the globus pallidus and occasionally the caudate nucleus. In severe advanced cases the genu of the internal capsule may be destroyed but it usually escapes. In acute cases there may also be cavities in the dentate nuclei and the frontal lobes, otherwise only pigmentation is seen in these areas.

Microscopically, the residual tissue in the areas of cavitation is found to be degenerated and is composed of fibres of varying size which stain irregularly.[1] The cavity walls are composed of a thick interlacing network of neuroglial cells, degenerated myelinated fibres and diseased blood vessels. The blood vessels in the area are not thrombosed or occluded and their walls, if anything, are thinner than normal. In the cerebral cortex a few of the Betz cells show pigmentary degeneration but there is no decrease in number.

In no case is there evidence of inflammatory reaction and the glial cell changes consist of various degrees of enlargement and proliferation of the astrocytes.[5]

In the pseudosclerotic form of the disease the lenticular nucleus appears grossly normal but microscopically there are large numbers of glial cells present with spread to adjacent areas of the brain. Restriction of the lesion to the lenticular nucleus never occurs and the fronto-parietal regions are often involved.[6]

Biochemical Manifestations

A prominent biochemical disturbance in Wilson's disease appears to be a defect in the synthesis of ceruloplasmin. This is an alpha-2-globulin with a molecular weight of 151,000 and it contains eight atoms of copper per molecule. In normal individuals 90–95% of the serum copper is bound to ceruloplasmin and 5–10% is bound to serum albumin. In the patient with Wilson's disease the ceruloplasmin is usually low with most of the serum copper present as a loosely bound albumin-copper complex. The sum of the two is usually lower than normal.

The level of serum copper varies in each patient because the actual level of ceruloplasmin varies in different patients. The rate of incorporation of radioactive copper into ceruloplasmin is markedly delayed in the patient suffering from Wilson's disease. Further studies utilizing radioactive copper have shown that in the normal individual 90% of an I.V. dose of Cu^{64} is concentrated in the liver ten hours following its adminstration and then the amount of radioactive copper in the liver gradually falls. On the other hand in Wilson's disease only 40–60% is taken up by the liver though uptake continues for at least sixty hours. These studies have also shown a disturbance in the mode of excretion of copper: a normal individual excretes more of the administered labelled copper in the stool than in the urine, the reverse is true in Wilson's disease where there is an increased urinary excretion of copper.

Associated biochemical abnormalities are aminoaciduria,[8] peptiduria, uricosuria, phosphaturia and glucosuria; these all seem to be secondary to renal involvement. The aminoaciduria is likely renal in origin because the blood amino acid levels appear to be normal. It is postulated that the aminoaciduria in Wilson's disease is a consequence of tubular damage secondary to copper deposition in the kidney.[15] Uzman[8] has shown a peptiduria which especially seems to involve alpha-amino nitrogen and N-terminal dicarboxylic amino acid residues. The glucosuria which is found in some patients is present in the face of a normal glucose tolerance test.[6] The uricosuria is accompanied by a low

serum urate level and a twice normal body uric acid turnover. The phosphaturia is due to an increased phosphate clearance by the kidney and is associated with a uniformly decreased serum phosphate level.[10]

It has also been noted that at least one third of the pathological copper found in the brain is in a form of copper-protein combination not found in appreciable amounts in the normal brain.[13]

Current Views on Pathogenesis

There are two currently accepted theories as to the cause of Wilson's disease.[7] The first is that the basic defect is a block in the production of ceruloplasmin and this, through some unknown mechanism, permits the absorption of increased amounts of copper from the intestine. As a result of the lack of ceruloplasmin the copper is in a highly diffusable form which is readily deposited in tissues, producing damage in certain organs and probably influencing Krebs cycle activity.

For a number of reasons neither of these theories can be accepted as yet. The first appeals to more investigators; both however fall far short of explaining all the known facts and it is felt by many that the nature of the basic metabolic defect in Wilson's disease is still in the realm of speculation.

Genetic Aspects

Wilson's disease is inherited in an autosomal recessive fashion in which the homozygote has the disease and the heterozygote, although clinically unaffected, may show some of the characteristic biochemical features of the disease. There is a high consanguinity rate among the parents of patients. According to Bearn,[14] who has studied thirty sibships with Wilson's disease, a first cousin consanguinity rate of 37% was obtained with a total consanguinity rate of 43%. No parents of patients have been found to be suffering from overt Wilson's disease. The ethnic background of the thirty families studied suggested that these cases may have arisen from a relatively few mutations occurring in the European part of Russia and in Sicily.

The primary expression of the abnormal gene is not known. The most constant biochemical abnormality is the presence of a low serum ceruloplasmin and this is fairly specific since it has not been found in any other neurological condition. The wide scatter of ceruloplasmin levels from zero to normal indicates it is not genetically homogenous and that there may be at least two types of Wilson's disease, one in which the metabolic block results in a lowered ceruloplasmin and one in which the level is near normal. Because of these considerations it probably would be wise to say that the abnormal ceruloplasmin level is merely a concomitant finding and not the primary defect.

Diagnosis

The diagnosis of Wilson's disease may be suspected on clinical findings but the diagnosis is confirmed by laboratory study, with the two together producing a picture of one of the forms of the disease.

Wilson's disease occurs in the first three decades of life.[6] The mode of presentation is either in the characteristic form with a mixture of both neurological and hepatic findings or it may be predominantly neurological or hepatic in nature. In the classical case the patient may present with any one of the neurological or hepatic findings and it is only on investigation that the full picture is elicited. The Kayser-Fleischer ring is an important part of the classical picture.

The neurological signs most commonly seen are those following disorganization of the lenticular nucleus. These are various degrees of tremor, rigidity, dysarthria and dysphagia. The tremor characteristically is a rhythmical flexion-extension movement at the wrist and in early cases it may be absent at rest.

Other unusual neurological signs have been noted. These are pyramidal in nature and occur only in advanced

cases. Rarely there are acute epileptiform seizures. There may be an acute left side paralysis with recovery in one to four weeks. There may be cortical damage with psychological sequelae, euphoria and inappropriate behaviour being prominent signs. The E.E.G. is normal except in late stages. About five percent of cases present in an acute form with the main signs being neurological.

Symptoms of liver involvement include those of being easily tired, and the presence of ascites and oedema; signs of liver disease are an enlarged, hard, nodular liver which later may be small, and possibly ascites and oedema. There are abnormalities of the liver function tests also. Splenomegaly is often associated with the liver disease and occasionally spider nevi may be noted. Rarely severe hematemesis is the presenting symptom.

In a large number of cases a Kayser-Fleischer ring is present and in any suspected case the patient's eyes must be examined with the slit-lamp since its presence is diagnostic. The Kayser-Fleischer ring is a greenish-yellow ring at the limbus of the cornea and is felt to be made up of pigment granules located in Descemet's membrane. It is not always complete and may be unilateral; rarely a second inner ring may occur. Frequently, the Kayser-Fleischer ring can be seen with the naked eye.

Laboratory Investigation

The investigation of Wilson's disease begins by the examination of various aspects of copper metabolism. The urinary output of copper is carefully noted and is usually found to be elevated in a twenty-four hour specimen. The levels of serum copper are also investigated. Both these procedures may be carried out by the method of Eden and Green.[11] The serum ceruloplasmin estimations may be performed using an immunochemical method devised by Cartwright.[12]

Aids to the laboratory diagnosis of Wilson's disease are an aminoaciduria, which may not be present in an early case, and uricosuria.

Liver biopsy may also be of value if a diseased area is obtained which shows the presence of lobules containing large amounts of copper and its characteristic distribution.

Bearn[16] in a systematic radiographic study of the bones of nineteen patients found significant abnormalities in thirteen. These consisted of severe degenerative changes around joints, especially in the spine, knees and elbows and there was an associated narrowing of the joint spaces even in young persons.

Forms of Wilson's Disease

The neurological form of the disease may present in one of two forms:

(a) The pseudosclerotic form presents with tremor as the only symptom.[6] Normal life continues for some time, the tremor gradually increasing. The rigidity, disorders of posture, dysarthria and dysphagia remain minimal.

(b) The opposite is true of the classical progressive lenticular degeneration. Rigidity, dysarthria and dysphagia dominate the picture with only minimal tremor.

The hepatic form presents with a firm, nodular liver, ascites and possibly jaundice. There may be some spider nevi and in the case of males, some gynecomastia. Later there may be esophageal varices. The laboratory aids show disturbances of liver function and a raised prothrombin time.

An acute form may occur in childhood and early adolescence; this has a rapidly progressive and malignant course with death in approximately eight months from the onset. It is frequently accompanied by a hectic swinging temperature for which no bacterial cause is found and which does not respond to antibiotics. The neurological symptoms predominate with a slight tremor progressing in a few weeks to an uncontrollable tremor and spastic rigidity. There is profound cachexia, a fixed facial expression and contractures of the limbs. There

is continuous drooling at the mouth and silly, childish, inappropriate laughter.

Treatment

The manifestations of this disease appear to be the result of the deposition of large amounts of copper in the tissues and therefore the aim of treatment should be directed toward lowering the total body copper volume. This appears to be the only avenue of treatment open to us at the present time in view of the fact that we do not know what the basic abnormality is and hence are unable to attack the disease at that level. This may be accomplished by removing as much copper from the body as is possible while maintaining copper absorption at a minimum by the use of diets low in copper and by giving something such as potassium sulphide[17] or a carbo-resin to inhibit absorption of copper into the body. The latter is necessary no matter what other forms of treatment are used.

The ideal therapeutic agent is one that can be given orally on a regular basis or in repeated courses for many years. It must be free of toxic side effects and must be readily soluble for rapid absorption from the intestine. It should have one or more stable -SH or other chelating groups and be readily excreted in the urine.

There are several substances available to aid copper removal. The first of these that was tried with any success is dimercaprol (BAL). This compound is successful in removing copper from the body, however, it is rarely able to produce a negative copper balance in the absence of toxic symptoms. BAL produces no improvement in cases of progressive lenticular degeneration; however, in the pseudosclerotic form there is marked neurological improvement although the cirrhotic process continues unchecked. Bearn[17] noted two groups of patients: (a) the BAL-sensitive group who were chronic cases and on low doses of BAL (200–300 mg. twice daily for many months) showed marked and continued improvement. There were many of these patients who showed toxic reactions. (b) the BAL-resistant group were the more acute cases and showed no improvement. Walshe has noted in some cases that the signs of hepatic dysfunction disappear though the cirrhosis continues.[7]

This drug, unfortunately, must be given parenterally and so presents a problem in long-term therapy. As well, there may be a painful local reaction. The toxic side effects of BAL may be quite marked at times; these are flushing of the face, nausea, vomiting, high fever, a rapid increase in neurological signs, hallucinations, temporary maniacal behaviour, sometimes coma and even death.

The next compound to be tried was Versene, the tetrasodium salt of ethylenediaminetetraacetic acid. This acts as a chelating agent to remove the copper and is reasonably effective, its disadvantage being that it must be given by I.V. drip in a large amount of isotonic sodium chloride solution and in interrupted courses. Then it was discovered that very good results could be obtained by a combination of Versene and BAL but it is not practical for the reasons stated above.[17]

Finally Penicillamine (B.B. dimethyl cysteine) was discovered and found to fit many of the requirements necessary for the treatment of Wilson's disease. Clinical trials show it to be a highly effective agent for the removal of copper from the body of patients with Wilson's disease. Its administration is followed by a large excretion of copper and it appears to lead to clinical improvement. Usually it is given orally but with certain precautions it can be given I.V. The only toxic effects thus far reported are one case of agranulocytosis[7] and in some cases, the development of a sensitivity reaction with fever, rash and itching.

In assessing the ability of a compound to remove copper from the body it must always be remembered that the excretion may be more apparent than real and that the compound may have become fully saturated with copper while

in the intestine and actually carry more copper into the body than is removed. In the case of Penicillamine the amount removed always exceeded the total daily intake by three or four times.

Prognosis

In spite of recent advances in therapy the prognosis is very poor with death occurring in five to ten years from onset. There have been some cases which have survived longer; however, these are in the minority. It is to be hoped that with use of the new drugs the prognosis will become brighter. At present there does not appear to be either a cure or a successful long term method of treatment. There is however a great deal of research being done at present and it is to be hoped that this will soon bear fruit.

Summary

The definition of Wilson's disease has been stated and its possible causes have been noted. The apparent underlying biochemical abnormalities have been outlined and their genetic foundation described. The pathology, especially that related to the liver and brain, is described. The diagnosis and investigation is set down along with the variations in presentation of the disease.

An attempt has been made to outline the treatment of this condition and the apparent success and ease of treatment with Penicillamine has been emphasized, though the value of BAL has not been minimized. The prognosis for this disease is, at present, not too encouraging though it is hoped that in the near future a reliable and convenient mode of treatment may be discovered.

Acknowledgement

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RESEARCH IN THE DEPARTMENT OF PHARMACOLOGY

R. O. DAVIES, Ph.D., 6T2

WHAT types of research does a pharmacologist undertake? What disciplines distinguish this worker from other medical scientists? These are common questions in the minds of persons viewing experimental fields of medicine and biology.

Generally, the pharmacologist is interested in elucidating the mechanism of action of drugs based upon physiological principles. The approach may include double blind clinical evaluation, anaesthesized animal preparations, isolated tissues and organs, and biochemical or cytological experiments. Adequate training in physiology, biochemistry, statistical methods, as well as pharmacology and toxicology are required.

Students from medicine and other faculties are accepted for postgraduate training and their problems may vary from clinical evaluation of drug action, to whole animal or tissue studies in the laboratory. One only has to look at the annual introduction of hundreds of potent therapeutic substances to appreciate the need and importance of pharmacology.

Research in the Department of Pharmacology is carried out under the direction of each of the four members of the professional staff, namely Professors E. A. Sellers, G. H. W. Lucas, W. Kalow and H. Kazant.

Professor Sellers, who was previously Chief Superintendent of The Defence Research Medical Laboratories at Downsview, and earlier a Professor of Physiology at the Best Institute, has been active in several fields of research. These include the endocrine system, particularly the thyroid gland, the effects of radiation, the induction of atherosclerosis by certain dietary factors, and the effects of exposure and acclimatization to cold. Some of this work is being extended by research teams in the Department of Pharmacology.

Mr. G. E. Johnson, who is working for a Ph.D. degree, is studying drugs and neurohormones which affect the metabolic rate and body temperature. It was found that reserpine caused both an early increase and a later fall in metabolic rate in the rat. The effect varies both with the dose injected and the ambient temperature of the animal. The early increase is attributed to release of catechol amines, and has been reproduced by injection of epinephrine. The effect is not due entirely to increased physical activity, since it can be demonstrated in phenobarbitone-treated animals. Studies also include drugs such as Marsilid and catechol which inhibit various enzymes involved in the metabolism of catechol amines. Secondly, the effect of this group of drugs is being examined in rats which are maintained at 30°C. and then suddenly transferred to 0°C. One of the effects of this shocking procedure is the release of catechol amines; some drugs alter this compensatory mechanism as observed by an alteration in the skin to rectal temperature gradient. Miss M. Metski is conducting research in this field, towards an undergraduate thesis, as part of a degree of Bachelor of Science in Pharmacy.

Research in cardiac function during hypothermia is being studied by Dr. R. O. Davies. From an isolated heart of rabbits, guinea-pigs and rats perfused according to Lagendorff, electrocardiographs from the atria and ventricles are recorded and electrical stimuli applied. Isometric tension during myocardial contraction is measured by a force transducer, and coronary perfusion by a drop counter. Function is measured during cooling, stimulation, drug administration, cold acclimatization and atherosclerosis.

Professor Sellers is collaborating with Professor E. Schönbaum of the Banting and Best Department of Medical Research in a study of the goitrogenic and

thyroid tumor-producing activties of a combination of propylthiouracil and thyroxin fed to rats over prolonged periods of time. Under these conditions the thyroid hormone enhances rather than antagonizes the goitrogenic effects of propylthiouracil. In animals fed a synthetic diet, free of iodide, rather than standard laboratory chow, the activity was less evident.

Professor Sellers has also taken part, with Dr. D. G. Baker of the Banting and Best Department of Medical Research, in short term feeding experiments on rats to study the induction of atherosclerosis in the coronary arteries.

Dr. Russell Taylor is studying respiratory function both in laboratory animals and in patients, and its modification by drugs. The clinical study is being conducted in the Cardio-Respiratory Laboratory of the Toronto General Hospital in co-operation with Dr. Colin R. Woolf. Basically, the study involves the measurement of pulmonary ventilation, gas mixing in the lungs, diffusion across the alveolar capillary membrane, and the effects of drugs and carbon dioxide on the medullary centres of respiration. Timed vital capacity measurements demonstrate the difficulty in exhalation commonly seen in asthmatic patients; residual air volumes are increased in emphysema. Faulty gas mixing, as seen in the emphysematous patient, can be detected by observing the pattern of "blow off" of either an administered volume of helium, or of nitrogen depletion after pure oxygen inhalation. Similar processes producing oedematous or fibrotic change in the alveolar capillary membrane are demonstrated by a reduced rate of absorption of carbon monoxide. Finally the central stimulating effect of carbon dioxide, with and without such drugs as nikethamide and leptazole, are being studied in cases of primary lung defects (emphysema), thoracic cage involvement (kyphoscoliosis) and central respiratory centre depression (barbiturate poisoning). Dr. Taylor has been doing similar types of experiments on animals in this laboratory.

Dr. Taylor has continued the studies begun by John Henderson and Ray Matthews, 6T0, during the summer of 1958 on the cardiac and respiratory toxicity of procaine in acute overdosage. With the assistance of Mr. Neil McPhail 6T1 during the summer of 1959, the effect was studied on rabbits receiving the intravenous procaine; death occurred very rapidly and was characterized by an acute drop in blood pressure. Pretreatment with such drugs as atropine, methoxamine and digitalis was of little value; concomittant administration of epinephrine saved the animal; pentobarbital as an anaesthetic lowered the toxicity to the animals. It is felt that death is due to the high concentration of procaine reaching and depressing the heart, before distribution throughout the body has taken place. The work is to be continued in co-operation with Mr. E. Chow, a new Master's candidate under Professor G. H. W. Lucas; determination of the concentration of procaine in samples removed by catheter from the heart during the fatal incident is to be undertaken.

The study of atmospheric pollutants, begun under Dr. Cullumbine and carried out formerly by Dr. H. Salem in co-operation with Dr. D. L. J. Bilbey of the Department of Anatomy is proceeding. Exposure to sulphur dioxide, an irritant toxic gas often found in polluted atmospheres, was found to be more toxic to guinea pigs than to mice; animals chronically exposed to sulphur dioxide developed resistance to the effects of the irritant; this was related to a stimulation of the reticulo-endothelial system as measured by the rate of disappearance of an intravenous dose of carbon particles. Mr. Martin Nash and Mr. Marvin Sazant, both of 6T1, were involved in this research during the summer months. Presently, the vulnerability of sensitized animals, due to pretreatment with antigenic substances such as egg white, is

being evaluated by Mr. Basil Leon in a Master's problem under Professor Sellers. Attempts to protect sensitized animals with drugs is contemplated.

Professor G. H. W. Lucas, the surviving member of the team (Lucas & Henderson) who discovered cyclopropane in 1928, is interested in problems related to anaesthesia and to various aspects of toxicology.

With Dr. C. Fabierkiewicz, he is investigating methods of identification of small amounts of tranquilizers including chlorpromazine, Frenquel, Atarax, reserpine, and meprobamate. These drugs can be identified by the morphology of the crystals formed by reaction with various heavy metal-containing precipitation reagents. Ascending paper chromatographs sprayed by color-producing reagents are also useful to separate the drugs and their metabolites.

Mr. M. Grossman has just completed an investigation into the etiological agent in poisonings and illness attributed to the consumption of green potatoes. Rather sketchy evidence has suggested that these incidents are due to an increase in the concentration of solanine, a steroidal alkaloid found in the potato. Mr. Grossman has developed an extraction procedure and both qualitative and quantative analyses for the alkaloid. Feeding tests in animals have failed to implicate solanine as a toxic agent; green potatoes themselves, fed to animals have failed to reproduce any untoward affects.

Mr. E. Chow and Professor Lucas are beginning a new series of investigations into the toxic properties of procaine.

Professor Lucas is cooperating with the Department of Electrical Engineering and The Defence Research Medical Laboratories in a study of the effects of barbiturates and tranquilizers on tests measuring co-ordination in man.

Professor Kalow has been interested in autonomic and biochemical pharmacology for some years. About six years ago Professor Kalow and Dr. D. R. Gunn of the New Toronto Mental Hospital investigated the familial incidence of prolonged apnea following small doses of succinylcholine given as a muscle relaxant before electric shock therapy. Professor Kalow discovered that the pseudocholinesterase in the serum of these patients failed to detoxify the drug; this was the first demonstration of a qualitatively altered form of an enzyme controlled by genetic mechanisms in man. Professor Kalow was invited to present his findings at the Ciba Symposium on Human Genetics in Naples in May 1959. The kinetics of this enzyme have been studied; the rate of hydrolysis of many substrates is substantially reduced, and the effect of many inhibitions is diminished. Presently the electrophoretic behaviour of the enzymic activity in starch gel is being investigated. There appears to be a mobility alteration to coincide with the kinetic differences, but the study is hampered by the rather rare occurrence of the enzyme in the population.

This interest in genetics and drug action is being expanded to include an investigation of the familial occurrence of symptoms of stimulation and excitement following morphine injections. With Dr. Gunn, an investigation of phenylketonuria in mentally retarded children from the hospital at Orillia is being undertaken; the possbile implication of catechol amine metabolism is to be studied. Other drug studies on a clinical basis are being considered locally.

Mr. T. S. Konop is conducting research towards a Ph.D. degree in a problem involving differences of some analgesic agents in various strains of mice. A standard method of inflicting pain, without trauma, involving electro shocks through the tail has been used; this enables the evaluation of analgesia, together with either resistance or tolerance developed after repeated injections. It is hoped to develop the problem towards a genetic study of drug action in animals. Also Mr. Konop is investigating the effect of protein binding as a route of detoxi-

fication for tubocurarine. The stimulating effect of acetylcholine on the rectus abdominis muscle of the frog is blocked by tubocurarine, and this effect is antagonized if the bath fluid contains blood serum.

Dr. A. Marton, who has just completed a Master's Degree in Pharmacology, is extending his work on the arylesterase of human serum. This esterase, to which no physiological function has as yet been assigned, hydrolyses *in vitro* such esters as phenylacetate and organo-phosphorus nerve gases and insecticides. The activity of this enzyme is greatly dependent on calcium ions; many activators and inhibitors likely act by competition with this cation. Dr. Marton is presently attempting to find optimum conditions for determination of the enzymic activity.

Professor H. Kalant, who joined the Department this fall, is continuing his research on biochemical problems at the cellular level. At Cambridge in 1956, Professor Kalant undertook to investigate the effects on cellular metabolism resulting from alteration of the intercellular cement substance by removal of calcium ions. This work was extended during his tenure at the Defence Research Medical Laboratories. Removal of calcium ions by perfusion of the liver of a rat with Versene or citrate produces a divided cell preparation, which though morphologically unaltered appears to have lost its selective permeability to sodium and potassium ions. When respiratory studies are conducted the cells appear to act as if without a membrane; there is loss of endogenous respiration but high sensitivity to respiratory stimulation by Krebs cycle intermediates when compared to a cell rich in calcium. Ehrlich ascites tumor cells do not show the same sensitivity to removal of calcium under these experimental conditions.

Secondly, Professor Kalant, who is also Director of Biological Research at the Alcohol Research Foundation of Ontario, is investigating the biochemical effects of acute alcohol intoxication. At present, studies on the disturbances in homeostatic mechanisms are focused on electrolyte changes in intra- and extracellular fluids. It is proposed to extend this work into such fields as glycolysis, active acetate and ketone bodies.

In summary, research in the Department includes the effects of drugs at various temperatures, respiratory function and drugs, air-pollution and drug treatment, toxicological studies, and biochemical effects of drugs. The effects are measured at all levels of organized function from the patient and laboratory animal down to single cells and body fluids.

Acknowledgement

The author gratefully acknowledges the interest and indulgence of the Professors and staff of the Department in providing material for this article.

Influenza Vaccine

During the winter of 1954–1955 a quadrivalent vaccine was tested. An epidemic of Influenza A (Cuppet 50) occurred which is one of the viruses incorporated in the vaccine. The study reveals protection varying from 40 to 80 per cent.

Pavilanis *et al.*: Influenza Vaccination, C.M.A.J. Oct. 1, 1959, Vol. 79.

Importance of Glaucoma

The authors performed 2,000 routine tonometric examinations. On the basis of their findings they report that:

(1) 3% of patients over 40 have glaucoma.

(2) 2% of patients over 40 have unrecognized glaucoma.

Extrapolating their results they estimate that 100,000 Canadians have unrecognized glaucoma. Because of this it is important that every physician should be proficient in the use of the tonometer, and use it routinely on all patients over 40.

Reed and Bendor-Samuel, C.M.A.J., Jan. 1, 1958, vol. 78, p. 9.

TESTICULAR NEOPLASMS

J. SCHATZKER, 6T0

Tumours of the testis are rare, and as such are neglected by most students in their quest for knowledge about "the common things which occur commonly". It is a sobering thought to realize that they are the commonest form of cancer in the male between the ages of 29 and 34.[1] This article will review some of the general features of testicular neoplasms, the diagnostic principles and the treatment.

Incidence

Tumours of the testis comprise 2% of all male carcinomas. They are more frequent in the cryptorchid testis (1:2,000) and in the dysgenetic gonads of the intersexes than in the normal testis (1:100,000).[2]

Etiology

As in all other forms of carcinoma the etiology is unknown. Since these tumours tend to occur at the period of greatest sexual vigor, it is probable that such activity and the increase in testicular hormones may be factors.[3] The finding of a gonadotrophin which shows principally FSH activity on bioassay in association with seminoma, may reflect the increased incidence of this tumour in patients with certain inherent testicular defects,[4] and this may indicate that the continual hormonal stimulation of the target cells may be an etiological factor.

Pathology

The cells of origin are the totipotent sex cells.[6]

Classification[4]

Primary tumours

I Germinal
1. Pure Seminoma.
2. Embryonal tumours.
   (a) Embryoma
   (b) Chorionepithelioma
   (c) Embryonal carcinoma
   (d) Teratocarcinoma
   (e) Adult teratoma.
3. Combination of 1 and 2 of the various types of embryonal tumours.

II Nongerminal tumours
1. Interstitial cell tumour.
2. Sertoli cell tumour.
3. Tumours of the testicular stroma, lipoma, etc.

Secondary tumours

I Lymphoma, plasmacytoma, leukemia, etc.

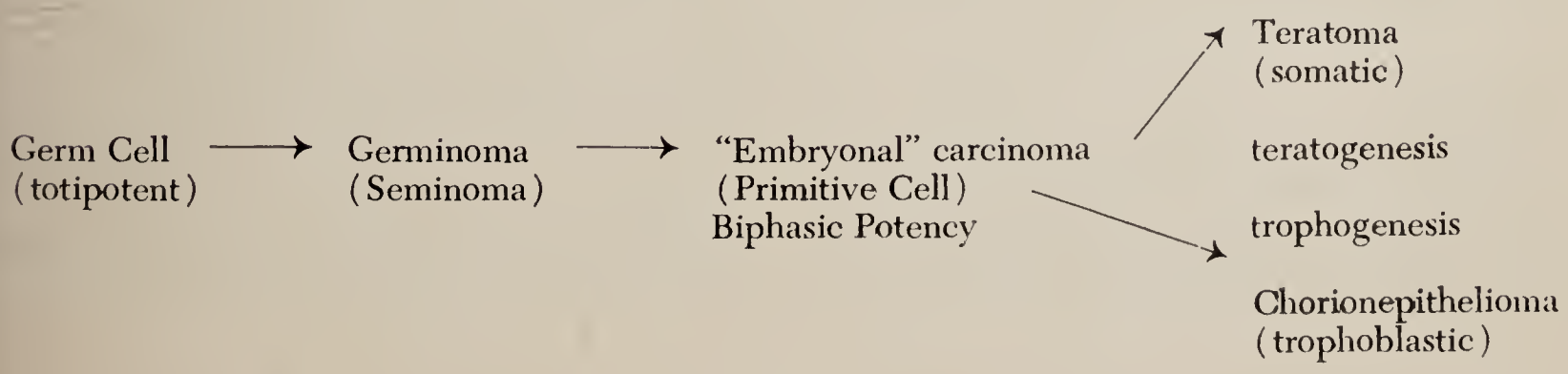
II Metastatic carcinoma.

The following is a table of the more common types, indicating their incidence and radiosensitivity.[7]

Type	*Incidence in %*	*Radiosensitivity*
1. Seminoma	46.9	Sensitive
2. Embryonal carcinoma	34.6	Resistant
3. Chorionepithelioma	1.5	,,
4. Teratocarcinoma	13.4	,,
5. Adult teratoma	2.5	,,
6. Miscellaneous	1.5	,,

Surg. Gyn. & Obs. 96:529, 1948

The fact that mixed types occur is well recognized. Seminoma, for instance, may be the precursor of embryonal carcinoma,



teratocarcinoma, and chorionepithelioma, and may metastasize in a similar fashion.

Seminoma.

Seminomas are mononuclear tumours which consist of rounded polyhedral cells, with clear cytoplasm and centrally-located hyperchromatic irregular nuclei. They grow in sheets, although separation of tumour masses by trabeculation of connective tissue may give rise to a pseudoglandular appearance. Lymphoid infiltration is variable.

Embryonal Carcinoma.

These tumours are composed of embryonal type cuboidal or columnar cells, which are larger than those of seminomas, and have a larger nucleus with clumped chromatin. The position of the nucleus within the cell varies. The differentiated part of the tumour is glandular in character, often assuming papillary formation; the undifferentiated parts often grow in solid sheets.

Chorionepithelioma.

These present a destructive picture comprised of compactly packed cytotrophoblastic cells and giant multinucleated syncytial structures which form an abortive reproduction of the placental villi. Extensive necrosis and areas of haemorrhage are frequent.

Teratocarcinoma.

These present the complex picture of an adult teratoma associated with a variety of malignant cell groups which may belong to any other tumour of germinal origin.

Adult teratoma.

These consist of differentiated adult tissue of ectodermal, endodermal, and mesothelial origin.

METASTASIS

Tumours of the testis metastasize both via the lymphatics and the blood stream. Lymphatic spread is more common, hematogenous metastasis appearing less often and usually later. The lymph trunks of the testicle ascend along the blood vessels of the spermatic cord. At the crossing point of spermatic vessels and ureter, the lymph vessels become separated from the internal spermatic artery and empty into the abdomino-aortic nodes. These are the most commonly involved nodes. From there further dissemination may take place via the thoracic duct with potential involvement of the mediastinum, lungs and supraclavicular nodes.

Hematogenous metastases most commonly settle in the lung. Other locations for hematogenous spread are the liver, adrenals, kidneys, pancreas, brain and bones.

Since there exists no connection between the testicular lymphatics and inguinal nodes, the involvement of the latter can occur only as the result of the primary tumour having extended into scrotal tissue.

SYMPTOMS

Local

Painless enlargement of the testis is the commonest symptom. Many patients notice the testicular enlargement while bathing and have no other symptoms. Discomfort usually becomes evident when the weight of the testis causes traction on the spermatic cord. Painless swelling is most often associated with seminomas. While if the swelling is painful, embryonal carcinomas or teratocarcinomas are usually the cause.

General

Weight loss, anorexia, abdominal pain, backache and persistent cough, with or without bloody sputum, are some distant symptoms indicating metastatic spread.

The more widely metastasizing embryonal carcinomas, teratocarcinomas, and chorionepitheliomas may first manifest themselves by their metastatic dissemination. Indeed, 80% of patients reported by Lewis with chorionepithelioma had metastases and in 50% of these the

metastases caused the presenting symptom.[5]

PHYSICAL FINDINGS

Local

1. A firm, diffuse and symmetrical swelling of the testis, which occasionally may be nodular, and most often is painless. The testis is heavy.
2. Rarely, the mass may be fixed to the scrotal skin.
3. At times associated hematocele, hydrocele or cyst is found.
4. The epididymis can usually be palpated separately, but may be involved in the spreading mass. The spermatic cord is usually not involved, but may be thickened and nodular at times, indicating involvement.

General

1. Lymphatic metastases.
   (a) midline abdominal mass (para-aortic group).
   (b) occasional enlargement of cervical nodes.
   (c) enlargement of iliac, inguinal and femoral nodes (not too frequent).
2. Pleural effusion.
3. Pulmonary consolidation.
4. Localized vertebral tenderness.
5. Gynaecomastia has been reported occurring with both germinal and interstitial tumours.

DIAGNOSTIC AIDS

1. X-ray examination.
   (a) Lungs—if metastases present, appear usually as multiple "cannon ball" lesions.
   (b) Excretory urography, and in certain cases retrograde pyelography to demonstrate lateral displacement or obstruction of ureters due to metastases in para-aortic lymph nodes. Hydronephrosis may also be noted.
2. Biopsy.

In no case should biopsy or needle puncture be resorted to as a means of establishing the diagnosis, because such a procedure would destroy the continuity of the capsule and facilitate dissemination of the tumour.

3. Aschheim-Zondek hormone test.

About 10% of patients with seminomas and about 25% of patients with other germinal tumours containing some chorionic tissue in them, excrete a gonadotrophin in the urine. This test, however, should not be used as a confirmatory test in the diagnosis of testicular tumours, since it is usually negative and may give a false sense of security. If it is positive it offers good supportive evidence. The amount of gonadotrophin secreted bears very little relationship to the size of the tumour.

DIFFERENTIAL DIAGNOSIS

Every mass in the scrotum should be considered malignant unless proven otherwise. Some of the conditions from which tumours must be differentiated are:

(a) Chronic non-specific epididymitis —especially when the urine is clear and the prostate and the seminal vesicles are normal. Diagnosing tumours as epididymitis or orchitis is the commonest diagnostic error.

(b) In tuberculosis, the testis has a tendency to become adherent to the scrotal skin with sinus formation. Also, the prostate and the seminal vesicles are usually involved with induration and irregularity. The urine usually shows pus cells. In tuberculosis or old gonorrheal epididymitis the epididymis is usually hard and nodular and the prostate and seminal vesicles may be involved.

(c) Syphilitic orchitis is usually accompanied by a positive serological test and a response to specific therapy.

(d) The forms of acute and chronic epididymo-orchitis.

(e) The various fluid-containing cysts such as hydrocele, haematocele

or spermatocele. These may be transilluminated and aspirated.

TREATMENT

The treatment of testicular tumours depends on the structural pattern and the biologic behaviour of the primary tumour and the presence, absence, or extent of metastatic disease. Removal of the primary tumour immediately after diagnosis is always indicated regardless of its histologic pattern and the presence of metastatic disease. This should be done through an inguinal incision. The cord is freed, ligated, and amputated at the level of the internal ring and the testis and cord are removed "en masse". Considering the high frequency of lymphatic metastasis it is advisable to treat lymph zones routinely despite the fact that metastases may not be clinically evident. If (a) the primary tumour shows embryonal carcinoma, teratocarcinoma, or chorionepithelioma, and (b) if there is no radiological or clinical evidence of widespread metastases, then a transthoracic route for a radical retroperitoneal lymph node dissection is advocated. If lymph node enlargement is found above the renal pedicle the tumour should be considered inoperable, and the procedure discontinued. After postoperative recovery, external irradiation should be given to all patients.

SUMMARY OF TREATMENT

(1) *Seminoma*:
Orchidectomy and external irradiation.

(2) *Other operable tumours*:
Orchidectomy, radical retroperitoneal node resection with postoperative external irradiation.

(3) *Inoperable tumours*:
Orchidectomy and palliative irradiation of tumour sites.

Biochemical agents have been tried in the therapy of germinal tumours. Female patients who have chorionepithelioma, may respond to folic acid antagonists but males do not respond.

PROGNOSIS

Prognosis is best in patients with seminoma or adult teratoma. The outlook is much more unfavourable in patients with embryonal carcinoma, teratocarcinoma or chorionepithelioma.

CASE

Mr. B.B. Age: 23 Admitted Sept. 30, 1959

Chief Complaint: Pain in right side of chest of 12 hours' duration.

History of Present Illness: This young man was perfectly well until two months before admission, when he began to feel tired and lose weight. Two weeks before admission he felt the sudden onset of pain in his right shoulder and right chest. The pain was sharp, increased by respiration and coughing and it lasted five minutes. On the day prior to admission he felt poorly, extremely fatigued and tired. On the night of admission he awoke suddenly from a deep sleep with a severe pain in his right chest anteriorly and posteriorly. The pain was of a similar character to the previous pain. He felt extremely ill, nauseated and prostrated. Four times he vomited small amounts of greenish fluid with globules of bloody mucus scattered in it. He denied any previous cough, hemoptysis, shortness of breath, tuberculosis contact, fever or chills.

History of Past Health, Functional Enquiry, and *Personal History* were noncontributory.

Physical Examination: The patient was a 23-year-old white man, well-built and well-nourished appearing pale and acutely ill. Head and Neck: no cervical lymphadenopathy. Chest: no dyspnoea or cyanosis; decreased movement on right side of chest; decreased vocal fremitus over lower right chest and right axilla; trachea shifted to left; dullness to percussion and decreased breath sounds over right lower chest. Cardiovascular System: pulse 100/min., regular; blood pressure 125/70. Abdomen: no palpable organs; palpable epigastric mass which was tender and transmitted aortic pulsa-

tion. Rectal examination: no abnormality noted. External genitalia: a smooth thickened raised area palpated on posteromedial aspect of right testicle; no other abnormality noted.

Laboratory Investigations: Urinalysis: negative. E.S.R.: 120 mm/hr. Hb.: 8.3 Gm.%. W.B.C. 12.7, with 84% polymorphs. Wasserman: negative. Blood culture: negative. O.T. #1: negative. L.E. cells: negative. A-Z test: positive.

Chest X-ray: Round circumscribed masses 4–6 cm., in diameter in both lung fields with generalized opacity in right lung field compatible with pleural effusion.

Thoracentesis yielded 0.5 cc. of blood. Direct smear: many red blood cells, few pus cells, no bacteria. Acid-fast smear: negative. Culture: no growth. Pathological report: considerable amount of blood, some swollen atypical cells with irregular foamy cytoplasm, eccentric nuclei and some large cells with nucleoli. Pattern compatible with mesothelial reaction to inflammation or with metastatic tumour.

Clinical Diagnosis: Chorionepithelioma of the right testis with widely disseminated metastases. The diagnosis was based on a positive A-Z test *with* a small primary tumour and widespread secondaries. Needle biopsy failed.

Clinical Course: Four days after admission the patient developed a left hemiplegia with loss of consciousness which was attributed to hemorrhage into a central nervous system metastasis. He went rapidly downhill and died fourteen days after admission.

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Combination of Antibiotics

The author presents a case of acute staphylococcal endocarditis secondary to a chronic dacryocystitis. The patient was placed on a combination of penicillin and erythromycin awaiting results of sensitivity tests, and on this regimen held her own. The sensitivity tests showed maximum susceptibility to Novobiocin, and accordingly, this antibiotic replaced the other two. Less than a day after replacement, the patient started a downhill course and died a few days later. The author feels that this is more than coincidence, and suggests that in treating serious staphylococcal infections, antibiotic combinations are advisable, and when a clinically successful formula has been found it should be persisted with until cure results or resistance develops. Changing the antibiotics to others which may be theoretically more successful may have unfortunate results.

D. M. Robertson, C.M.A.J. Aug. 1, Vol. 79.

The importance of routine health check-ups is emphasized by these figures: 25 to 35% of adult males examined for the first time were found to have a significant disease not known to have existed previously. Periodic examinations are therefore a necessity in detection of diseases at an early reversible or arrestable stage, as well as providing a baseline on which future examinations can rely.

N. J. Roberts, J. Chron. Dis. 9:95, 1959.

THE ACADEMY OF MEDICINE, TORONTO

RICHARD M. GLADSTONE, 6T4

Formation and Development

The first medical society in Toronto was the Medico-Chirurgical Society of Upper Canada, which was organized in 1834 with Christopher Widmer as President. In 1839 a Provincial Act set up the College of Physicians and Surgeons of Upper Canada. However, this Act was disallowed by the Imperial Parliament and so the library of the College of Physicians and Surgeons was transferred to the Medico-Chirurgical Society for safe-keeping. In 1887 the Ontario Medical Library Association was organized and in 1889 the Toronto Pathological Society came into being. On the initiative of Dr. G. Sterling Ryerson, the Toronto Clinical Society was organized in 1892.

In 1904 the Ontario Medical Library Association acquired from the University the property at 9 Queen's Park to which the Library was transferred. The members and interested friends collected $5,000.00 for the purchase of the building and this sum was generously duplicated by another $5,000.00 from the Massey estate.

In consequence of this development all four of the medical organizations then existing in Toronto had their headquarters and meetings in the same building although each continued to retain its identity through the collection of its own dues, the election of its own members and the arrangement of its own programmes. This new Library Building on Queen's Park, a convenient location, soon became the unofficial headquarters of the medical profession, where medical meetings were held and members of the profession came to consult books and journals. That these were still the days when the doctor visited his patients in a brightly polished buggy with a well-groomed, high-stepping horse, is clearly indicated in the minutes of the Library Association meeting of October 27, 1905 —"Dr. Machell pointed out the convenience of having a tie-post in front of the Library and offered to put one in. His offer was approved and accepted."

For many years there was a movement toward amalgamation of these four societies, in order to improve the quality of the meetings, to increase the corporate influence of the profession and to promote the development of the library. This idea had the hearty support and cooperation of many leading men in the medical profession, including Sir William Osler. In December 1906, Osler delivered and published a paper on "The Educational Value of the Medical Society" which greatly stimulated the idea. Amalgamation took place in 1907, uniting by unanimous consent the members of the Toronto Medical Society, the Toronto Pathological Society and the Toronto Clinical Society, with the Ontario Medical Library Association as its nucleus. The original Declaration for Incorporation of The Academy was signed on February 20, 1907, by 19 members, who were the Executive Officers of the societies concerned. The Academy was then organized under Provincial Charter and on May 31, with Dr. J. F. W. Ross as President, held its first meeting in the new Medical Building, University of Toronto.

The Academy moved to 13 Queen's Park when the University appropriated 9 Queen's Park for a student residence. In 1921 the addition of Osler Hall with a large reading room above it was realized through funds secured by subscription of the membership. Here the Academy remained until 1946 when the Ontario Government purchased the building to house the Provincial Police. At this time the membership had exceeded the facilities of these premises. A large private residence at 288 Bloor St. West was purchased and although not

as convenient to the University or the city hospitals, this location has proved quite suitable until the present. Since the Academy essentially subserves an educational function, a bill was passed by the Provincial Government making this property tax-exempt.

On April 21, 1951, the Honorable Herbert A. Bruce laid the cornerstone of a new building on the property which, designed to accommodate three additional storeys, presently houses a 340-seat auditorium, a basement of library stalls, and a Board Room on the second floor. On November 16, 1951, this addition was officially opened by the late Dr. W. E. Gallie.

Activities and Functions

In 1934, in celebration of the sesquicentennial of the Province of Ontario and the centennial of the City of Toronto, the Academy began a collection of apparatus, instruments, appliances, documents and other objects of medical interest in the history of the Province. This collection has grown into a valuable museum which is used for teaching purposes for undergraduates in medicine. The Academy Museum contains things of sentimental interest and other items of such rarity that they would be impossible to replace. It has an infant feeding apparatus and amulets dating back to 400 B.C. It houses the Osler Collection, Dr. James Bovell's stethoscope, Semmelweis' original midwifery basin, the original Lister spray, Dr. Beaumont's automatic needle-threader, a gold watch presented to Dr. John Rolph in 1837, and many pictures and medals, including those of the late Sir Frederick Banting.

The Academy has shown a steady increase in membership since its beginning in 1907, at which time there were 187 Fellows. In 1957, the 50th Anniversary of the Academy was celebrated and at that time the Academy numbered 2,061 Fellows.

During the same period The Academy library has had a parallel growth having increased from 4,602 volumes in 1907 to over 40,000 in 1957, with 1000 accessions a year. The library also contains an excellent reference and duplicating service. The library has a special section on the History of Medicine. A Rare Book section with many prized acquisitions is housed in the basement of the Academy. There is a monthly exhibit of items from this collection. In 1956 a Historical Book Committee was formed to supervise the care and purchase of rare books. The Portrait Section of the Library was started in 1916 by Dr. John Ferguson. All portraits in the Academy and pictures of important men in medicine that may be found in texts or journals are indexed here.

In 1925 the Academy installed its first telephone switchboard. At that time the Academy undertook to provide an emergency service for the public. Since then it has maintained a list of physicians who will answer emergency calls, and the switchboard will send a doctor in response to any urgent call received. At the time of the tragic fire on board the passengership, Noronic, in Toronto harbour the Academy operators were asked to find doctors to tend the many injuries which occurred. The emergency service has been used by the Civil Defence organization and the full facilities of the switchboard will be placed at the disposal of the Civil Defence authorities in the event of a disaster in this area.

In 1937 Dr. R. M. Heard made arrangements with the Bell Telephone Company to establish a Call Answering Service for Toronto physicians. This has operated as a separate department on a non-profit basis and is completely self-supporting. There are over 300 Fellows who use this service and the switchboard handles about 300,000 calls per month. These calls are handled through 6 switchboards located on the third floor of the Academy, giving service to the entire Metropolitan Toronto area. In order to provide a 24-hour coverage the

Academy employs 18 full-time and 4 part-time operators.

Because of the increase in size and circulation of the Library, the rapid increase in the number of items in the Museum and the increased staff required, the Executive Committee and Council have been considering the need for physical expansion of the premises in the near future. For this purpose, a Planning Committee was formed in 1957 to consider and plan for the requirements of the Academy for the next 50 years.

The present Fellows of the Academy and its Executive continue to fulfil the original intent of its founders:

"The purposes of the Academy shall be the advancement of the art and science of medicine with its collateral branches; the promotion and maintenance of an efficient library and museum; professional improvement; the cultivation of harmony and good feeling among its Fellows; and the promotion of the corporate influence of the profession in relation to the community."

Material for this article was taken from the Bulletins of the Academy of Medicine in May 1932 (Silver Jubilee) and April 1957 (50th Anniversary) and The Acts of Incorporation, By-laws and Rules and Regulations of the Academy (1958).

Dangers of Hypodermoclysis in Infancy

The authors here report a case of severe vomiting and diarrhoea in infancy, which terminated fatally. The authors postulate that the child was suffering from acute hypovolemia with consequent oliguria. By hypodermoclysis an extra fluid compartment is provided into which more fluid can enter from the intravascular compartment, since this is in fact a hypertonic space. This occurence provides the death blow to an already decompensated renal flow. They suggest that where fluid replacement is vitally necessary, it should be given intravenously.

S. Israels, K. Wylie, C.M.A.J. 80:1, p. 31, Jan. 1. 1959.

Meprobamate Addiction

Meprobamate is said to be virtually free from addictive properties. However, in patients who have been previously addicted to other drugs, addiction may occur to this drug as well. The authors describe the case of a male alcoholic who was treated with barbiturates. When he became addicted to these they were replaced by meprobamate. On admission to hospital he was taking fifty 400 mg. tablets daily, and on withdrawal developed a severe grand mal seizure and medication had to be restarted temporarily.

Mohr and Mead, New Eng. Med Journ. 259:865, 1958.

Steroids and Anticoagulants

Singly, ACTH is known to increase the number of circulating platelets and decrease capillary fragility. The authors performed a double blind study on rabbits. A significant number of rabbits treated with both ACTH and dicoumarol died of haemorrhages from the gastrointestinal, pulmonary and urinary systems. No animal died of ACTH treatment alone, and very few on dicoumarol alone. (Cortisone, somatotrophin and DOCA did not produce the same effects as ACTH.) The application of this experiment to humans is exemplified by a case of gross phlebitis of the right leg associated with acute rheumatoid arthritis. The phlebitis was treated with dicoumarol, and the arthritis with ACTH. An extensive gastrointestinal haemorrhage resulted which stopped with cessation of therapy. No lesion which could account for this could be found.

Van Cauwenberge and Jacques: ACTH and Anti Coagulants, C.M.A.J., Oct. 1, 1958. vol. 79, p. 538.

ABSTRACTS

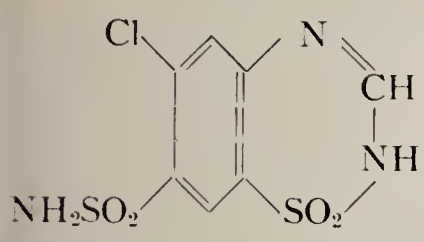
HYDROCHLOROTHIAZIDE, A COMPARISON WITH CHLOROTHIAZIDE. Fleming, Zilva, Bayliss, Pirkiss. The Lancet. No. 7085. June 13, 1959.

The introduction of chlorothiazide (Diuril) was an important advance in the treatment of oedema, because this was the first oral diuretic comparable in potency to parenterally administered mercurials. Chlorothiazide induces diuresis chiefly by enhancing the urinary excretion of sodium and chloride. It may also promote the excretion of bicarbonate and potassium—an effect attributed to mild carbonic-anhydrase inhibition. This increased loss of potassium with liability to potassium depletion and hypokalaemia makes intermittent treatment advisable and often necessitates the concurrent administration of a potassium supplement.

Recently hydrochlorothiazide has been introduced. This differs from chlorothiazide in having the double bond in the heterocyclic ring saturated with two hydrogen atoms. This study was made to determine whether there was clinically any difference in the diuretic actions of chlorothiazide and hydrochlorothiazide, to assess their relative potency, and to establish the therapeutic value of hydrochlorothiazide. A series was run on four patients convalescing from conditions unaccompanied by oedema, six healthy ambulant subjects, and ten oedematous patients suffering from a variety of conditions.

Hydrochlorothiazide was shown to be an effective diuretic. In healthy subjects it is weight for weight, some twenty times more potent than chlorothiazide, as regards sodium and chloride excretion, although the amount of urine passed was not significantly larger. In oedematous patients there are considerable individual variations, but usually hydrochlorothiazide is some ten times more potent than the parent compound.

Hydrochlorothiazide promotes less bicarbonate excretion than chlorothiazide, but the loss of potassium after the two drugs is not significantly different. For this reason hydrochlorothiazide should be given intermittently, and when treatment is continued for more than a few days supplements of potassium chloride are necessary.



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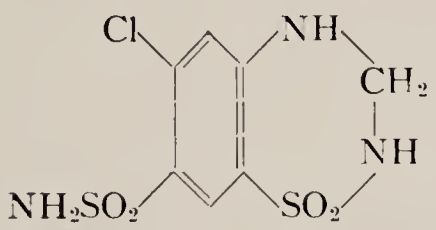

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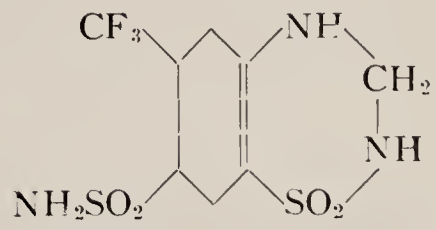


HYDROFLUMETHIAZIDE

E.J.H.

HYDROFLUMETHIAZIDE, A NEW ORAL DIURETIC. C. J. Edmonds and G. M. Wilson. The Lancet. No. 7098. September 12, 1959.

Hydroflumethiazide (Hydrenox) is an oral diuretic related chemically to chlorothiazide. In comparison with chlorothiazide in normal subjects it was active in about one-tenth the dose, caused a more prolonged diuresis of water and sodium, and produced less bicarbonate but more chloride excretion. Its action closely resembled that of hydrochlorothiazide.

In a clinical study of thirty patients, hydroflumethiazide was an effective diuretic in the majority. Where it failed chlorothiazide was also ineffective, but mersalyl was occasionally successful.

Failure to respond was usually associated with impaired renal function, as shown by an elevated blood urea.

Hypokalaemia in a few cases was the only side-effect encountered.

E.J.H.

THE CHROMOSOMES IN A PATIENT SHOWING BOTH MONGOLISM AND THE KLINEFELTER SYNDROME. C. E. Ford, K. W. Jones, O. J. Miller, U. Mittwoch, L. S. Penrose, M. Ridler and A. Shapiro. The Lancet. No. 7075. April 4, 1959.

For many years the diploid number of chromosomes in normal men and women was believed to be forty-eight. However, at present, with the use of improved methods of determination, forty-six has been generally accepted as the correct number, twenty-two pairs of autosomes and one sex chromosome pair. The chromosomes of a case of Klinefelter's syndrome, with skin cells exhibiting the Barr chromatin body as in the female have been found to number forty-seven by Jacobs and Strong (1959). This was interpreted as the result of the presence of two X chromosomes as well as one Y.

Lejeune, Gautier, and Turpin (1959) reported the finding of a small acrocentric extra chromosome in tissue cultures from the connective tissue of three cases of mongolism, making a total count of forty-seven.

The patient described by the authors is an imbecile, aged forty-five, who shows signs typical of both Klinefelter's syndrome and mongolism. The Barr chromatin body is present in cells of the skin and buccal mucosa; leucocytes with drumstick appendages have been identified, as in a normal female. He has small testes, scanty facial, axillary, and pubic hair, slight gynaecomastia and feminine distribution of fat. Testicular biopsy revealed advanced atrophy with no spermatogenesis. The mongoloid traits are very well marked, including typical palmar patterns, single creases on the minimal digits, fissured tongue, cataract, and slight cyanosis.

Bone marrow specimens were searched systematically for cells in metaphase of mitosis. More than fifty cells, in which the chromosomes could be counted accurately, were recorded, and each contained forty-eight chromosomes. The detailed chromosome morphology was examined carefully in ten cells. Each appeared to contain a normal set of twenty-three pairs, as in a female, with, in addition, a Y chromosome and an extra acrocentric chromosome.

This appears to be the first time a human being with two supernumerary chromosomes has been described.

E.J.H.

ANTICOAGULANTS IN STROKES

In haemorrhagic strokes the use of anticoagulants could be disastrous. In thrombotic occlusion of minor vessels they have no effect and the side effects contraindicate their routine use here. Proper indications are:

(1) The syndrome of intermittent insufficiency of the vertebral-basilar artery system.
(2) The syndrome of intermittent insufficiency in the carotid artery.
(3) Thrombosis in the vertebral-basilar artery system.
(4) Slow stroke (stroke in evolution).
(5) Thrombo-embolic disorders.

Millikan *et al.*, Med. Clin. of N.A. p. 939, July, 1958.

NEWS AND NOTES

Dr. W. Bernhard who works at the Institute de Recherches sur le Cancer, near Paris, France, lectured on "Ultrastructure of Tumor Cells and Tumor Viruses. Facts and Problems." The lecture took place on November 25 at the Ontario Cancer Institute. Dr. Bernhard has a world-wide reputation for his investigations on the fine structure of cells and viruses by electron microscopy.

John R. Brown, formerly lecturer in Applied Physiology at the London School of Hygiene and Tropical Medicine, University of London, has been appointed Professor and Head of the Dept. of Physiological Hygiene in the School of Hygiene. Dr. Brown will be responsible for developing the recently reorganized program of postgraduate teaching for industrial and public health physicians.

C. W. Schwenger has been appointed assistant Professor of Public Health. A Toronto graduate, Dr. Schwenger trained in England and the United States, and earned his diploma in Public Health here in 1954. He has been director of the Dufferin County Health unit.

The International Students Organization and the Varsity Christian Fellowship sponsored a lecture by Dr. Khoo Don Terk, Senior Lecturer in Clinical Medicine at the University of Malaya. On November 8 Dr. Terk spoke on "Problems of Clinical Medicine and Christian Ethics in Southeast Asia."

Hoechst Pharmaceuticals of Canada Ltd. marked National Diabetic Week (November 14–21) by granting $5000.00 to the Banting and Best Institutes, University of Toronto. The grant was announced by Dr. Giese, Scientific Director for Hoechst, who said that its purpose was to facilitate research on carbohydrate metabolism and experimental diabetes. A grant of $3000.00 was made to the Institute by the same company last February.

The William Osler Medal of the American Association for the History of Medicine is awarded annually for the best unpublished essay on a medico-historical topic written by a student in a medical school in United States or Canada. The medal commemorates the great physician Sir William Osler (1849–1919) who generated a love for the humanities among students and doctors alike.

Essays should not exceed 10,000 words and should demonstrate either original research or an unusual understanding of a medico-historical problem. The prize-winning essay may be considered for publication in the Bulletin of the History of Medicine, which is the official organ of the Association. The next deadline is April 1, 1960. Essays must be submitted to Dr. S. X. Radbill, 7043 Elmwood Ave., Philadelphia, Pa.

Special Lecture – "The Effects of Strontium 90 on Teeth and Jaws" was given by Prof. A. M. Rushton of Guy's Hospital, London, England on November 24 at the new Dental Building.

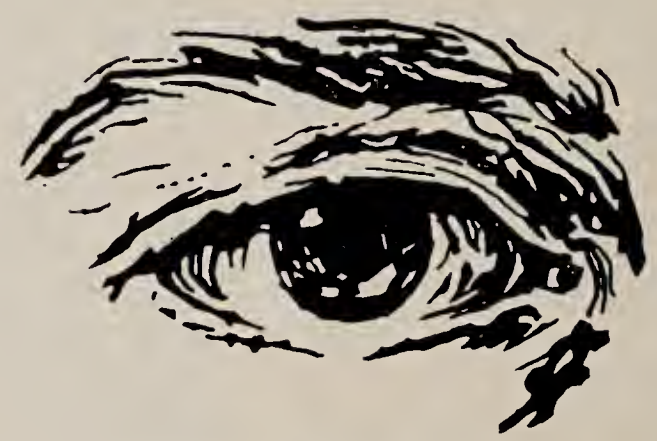
The Academy of Medicine held their Stated Meeting on December 1 in Osler Hall. The guest speaker was R. C. Dickson who is Professor of Medicine at Dalhousie University. Dr. Dickson spoke on "Heartburn."

Dr. James Q. Bliss, former editor of this journal, who graduated from U. of T. Medical School in 1956 won a Post-Doctoral Fellowship to study with Dr. Peter L. Krohn at the University of Birmingham, England.

The lectures for the Varsity Christian Fellowship Mission at the University of Toronto in November had a special appeal for medical students. On November 10 Dr. Orville Walters, Director of Health Services at the University of Illinois, spoke on the topic "A Psychiatrist Evaluates Christian Faith." The chairman of the discussion that followed was Dr. R. E. Haist, Professor of Physio-

logy at the University of Toronto. On November 12, Dr. C. P. Martin, Professor Emeritus of Anatomy at McGill University spoke on "The Decline of Religion". Chairman of the discussion was Dr. J. W. A. Duckworth, Professor and Head of the Department of Anatomy at the University of Toronto. On November 13, Dr. Gwyn Walters, Professor of Christian Ethics at Temple University spoke on the topic "Ethical Problems of the Specialist." The chairman of the discussion was Dr. E. A. Sellers, Head of the Department of Pharmacology at University of Toronto.

Dr. Charles H. Best received the degree of Doctor of Laws from Edinburgh University at a special ceremony held in conjunction with the conference of the British and Canadian Medical Associations in Edinburgh in the summer. Dr. Best also received an honorary D.Sc. degree during a Convocation commemorating the 100th anniversary of the founding of Northwestern University Medical School. Dr. Best spoke at the Colloquium of Medical Sciences on "Unfinished Researches."



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Eradicates or prevents growth of both gram-negative and gram-positive pathogens — without mucosal irritation.

Contains no antibiotic

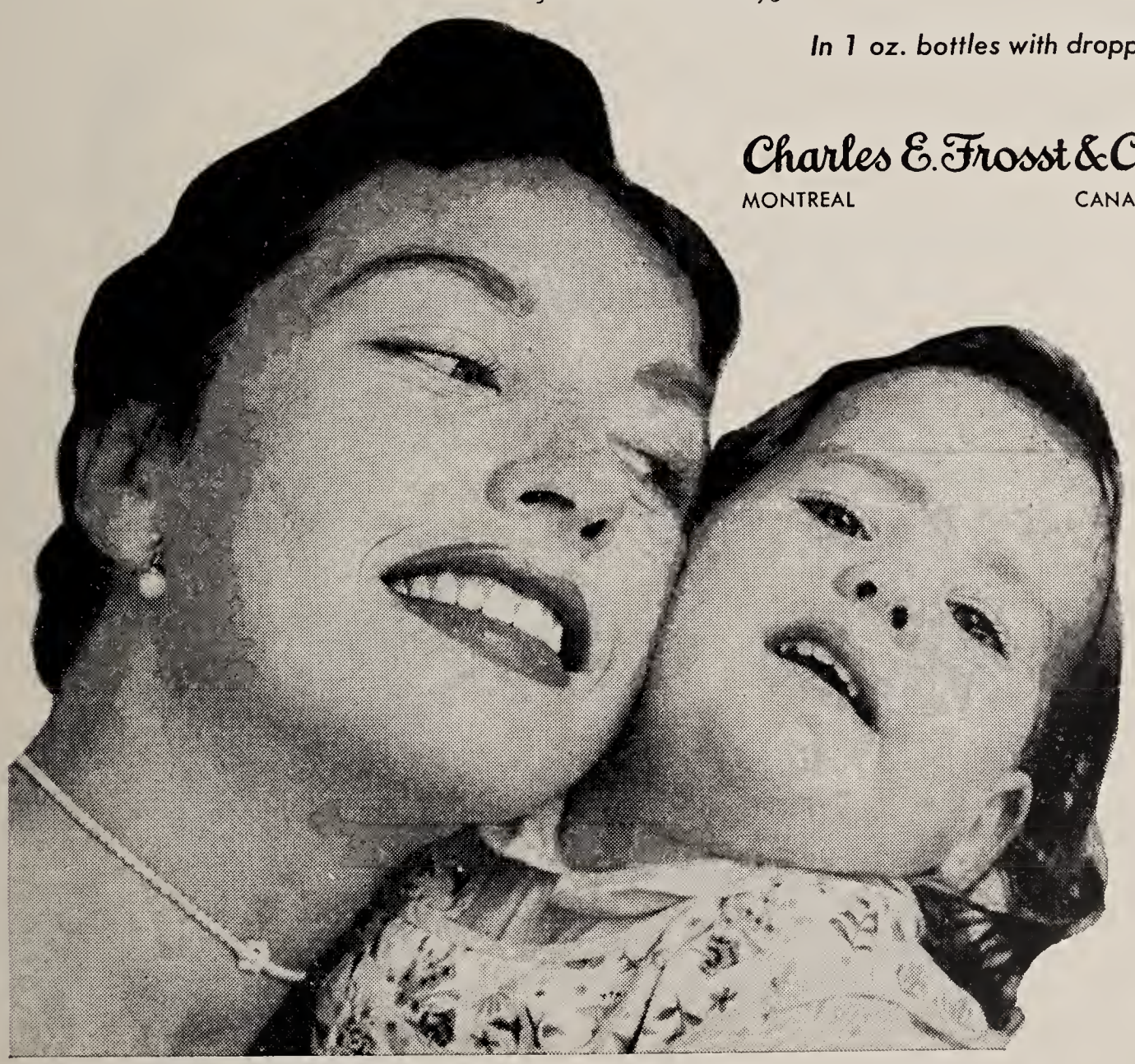
FORMULA: Ephedrine hydrochloride, 0.3% and aminacrine hydrochloride, 0.1%, in an aqueous isotonic solution.

ADMINISTRATION: To relieve nasal congestion in allergic, inflammatory or infectious disorders, instil 3 or 4 drops into each nostril every 3 or 4 hours.

In ½ oz. bottles with dropper.

ALSO AVAILABLE . . . **"FLAVEDRIN"**
Ephedrine hydrochloride 1.0% and aminacrine hydrochloride 0.1%.

In 1 oz. bottles with dropper.



Charles E. Frosst & Co.
MONTREAL CANADA

Lederle introduces

DECLOMYCIN®

Demethylchlortetracycline Lederle

a masterpiece of antibiotic design

Derived from a strain of *Streptomyces Aureofaciens*, DECLOMYCIN is the latest in the distinguished company of Lederle antibiotics. *Streptomyces Aureofaciens* is also the parent organism of AUREOMYCIN® Chlortetracycline and ACHROMYCIN® Tetracycline. AUREOMYCIN was first introduced by Lederle in 1948 and quickly became synonymous with "broad spectrum antibiotic."

In 1953 ACHROMYCIN was introduced and became the most widely prescribed antibiotic in the world. Now Lederle research leads again with DECLOMYCIN Demethylchlortetracycline.

DECLOMYCIN is superior to tetracycline in:

—Supplying far greater antibiotic activity with far less antibiotic.

—Maintaining antibacterial activity for one to two days after the last dose.

—Eliminating peak and valley fluctuation of—antibiotic level in body fluids.

strikingly enhances the traditional advantages of broad spectrum antibiotics

Available as:
Capsules—150 mg.
Pediatric Drops—60 mg./c.c.
Oral Suspension—75 mg./5 c.c.

® Reg. Trade Mark in Canada

Lederle CYANAMID OF CANADA LIMITED *Montreal*

TIME through the ages

WATER-CLOCK

Such clocks were used in the Athenian law courts to mark the time allotted to speakers. They were introduced in Rome around 159 B.C. and used in the courts there in the same way. The best clock of this type is attributed to Plato.

TIME to relax

By using the complete dispensing service offered by your pharmacist, you free yourself of the needless detail and expense of running a dispensary; enabling you to follow the advice you give your patients and take time to relax.

LET THE PHARMACIST
DO ALL YOUR DISPENSING

ONTARIO RETAIL PHARMACISTS ASSOCIATION

THE ONTARIO RETAIL PHARMACISTS' ASSOCIATION